ANKLE BRACHIAL INDEX AS A PREDICTOR OF SILENT MYOCARDIAL ISCHEMIA IN ASYMPTOMATIC TYPE 2 DIABETES MELLITUS PATIENTS

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CERTIFICATE

This is to certify that this dissertation entitled "**ANKLE BRACHIAL INDEX AS A PREDICTOR OF SILENT MYOCARDIAL ISCHEMIA IN ASYMPTOMATIC TYPE 2 DIABETES MELLITUS PATIENTS"** is a bonafide work done by **Dr. S. RAJ KUMAR,** Post Graduate Student, Institute of Internal Medicine, Madras Medical College, Chennai – 3 in partial fulfilment of the University Rules and Regulations for the award of M.D. Branch – I General Medicine, under our guidance and supervision, during the Academic period from May 2011 to November 2011.

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DECLARATION

I, **Dr. S. RAJKUMAR** solemnly declare that the dissertation entitled "**ANKLE BRACHIAL INDEX AS A PREDICTOR OF SILENT MYOCARDIAL ISCHEMIA IN ASYMPTOMATIC TYPE 2 DIABETES MELLITUS PATIENTS**" is done by me at Madras Medical College, Chennai – 3 during the period May 2011 to November 2011 under the guidance and supervision of **Prof. P. CHITRAMBALAM M.D.** to be submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfilment of the requirements for the award of M.D. DEGREE (Branch - I GENERAL MEDICINE).

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ABBREVIATIONS

CAD	:	Coronary Artery Disease
CVD	:	Cardio Vascular Disease
SMI	:	Silent Myocardial Ischemia
ABI	:	Ankle Brachial Index
PAD	:	Peripheral Artery Disease
TMT	:	Tread Mill Test
WC	:	Waist Circumference
W/H	:	Waist Hip Ratio
BMI	:	Body Mass Index
ECG	:	Electrocardiography
ADA	:	American Diabetes Association
ACC	:	American College of Cardiology
AHA	:	American Heart Association
MI	:	Myocardial Infarction
CABG	:	Coronary Artery Bypass Graft
PTCA	:	Percutaneous Transluminal Coronary Angioplasty

CONTENTS

INTRODUCTION

Diabetes is an important risk factor for the development of coronary artery disease (CAD). CAD accounts for about 70-80% of death in diabetic patients[1,2]. Patients with diabetes develop CAD at an accelerated rate and have a higher incidence of heart failure, myocardial infarction, and cardiac death compared to non-diabetics[3]. Moreover, compared with non-diabetic patients, diabetic patients have lower ejection fraction and more frequent silent myocardial infarction[4-9].

Diabetic patients have a more extensive coronary atherosclerosis and their epicardial vessels are less amenable to interventional treatment compared with the non-diabetic population[10-12]. These findings can easily explain the poor outcome of these patients. CAD in diabetic patients is detected at an advanced stage, whereas the disease in its premature, asymptomatic stages remains undetected because the typical anginal symptoms are often masked[13]. As a consequence, multivessel atherosclerosis is often present before anginal symptoms occur and before treatment can be instituted[14-15]. Undoubtedly a delayed recognition of CAD worsens the prognosis for survival. So an effective and aggressive strategy for early detection of subclinical CAD could lead to a more effective prevention and can reduce morbidity and mortality in these patients.

One of the diagnostic tools for the diagnosis and risk stratification of coronary heart disease is exercise stress testing, whose diagnostic and prognostic value has been studied extensively. Electrocardiograph (ECG) exercise stress testing is a reliable and widely used method for evaluating patients who are at increased risk of developing cardiovascular disease. The predictive value of the exercise stress test is greatest when test results are combined with family history, current cardiac symptoms, and underlying risk factors. Combining clinical information with test data yields a 94% sensitivity and 92% specifcity.[16]

Many studies have demonstrated that a significant percentage of patients with diabetes who have no symptoms of CAD have abnormal stress tests, either by stress ECG, stress echocardiogram, or stress nuclear perfusion imaging. It has also been demonstrated that patients with silent myocardial ischemia have a poorer prognosis than those with normal stress tests, and their risk is further increased if cardiac autonomic neuropathy coexists.[17]

So as the number of individuals who develop diabetes increases in developing countries like India, more patients will need to undergo detailed cardiovascular assessment. Although diagnosing and treating patients with diabetes and associated CAD is essential, the proper screening method for detecting the disease and its evaluation remains a constant challenge.

PAD is a common problem in diabetic patients and it has the ability to predict future cardiac events in these individuals. The role of the ankle/brachial index (ABI) in the detection of asymptomatic PAD, especially in diabetic individuals, is well established[18,19].

The American Diabetes Association (ADA) quotes the normal range of ABI as being 0.91–1.3[20]. An ABI of ≤0.90 is 95% sensitive and 99% specific for angiographically documented PAD. The specificity of low ABI for coronary heart disease, stroke, and cardiovascular mortality was 92.7%, 92.2%, and 87.9%, respectively. ABI >1.40 predicts mortality with similar strength as ABI ≤0.90.It's not just about the legs, in asymptomatic individuals, the ABI should be thought of as a biomarker of cardiovascular disease risk[21].

So it's high time to assess the ABI as a predictor of silent myocardial ischemia in asymptomatic type 2 DM patients hailing from India so that we can identify those who are at increased risk of future cardiovascular events earlier. By instituting the appropriate therapy we can decrease the mortality and morbidity in these patients.

AIMS AND OBJECTIVES

AIM

To asses ankle brachial index (ABI) as a predictor of silent myocardial ischemia in asymptomatic type 2 DM patients.

OBJECTIVES

PRIMARY

1. To measure ankle brachial index (ABI) using hand held Doppler in asymptomatic type 2 DM patients.
2. To assess the presence of silent myocardial ischemia (SMI) in asymptomatic type 2 DM patients.
3. To evaluate the relationship between ankle brachial index (ABI) and silent myocardial ischemia (SMI) in asymptomatic type 2 DM patients.

SECONDARY

To assess the risk factors associated with development of silent myocardial ischemia in asymptomatic type 2 DM patients.

REVIEW OF LITERATURE

Cardiovascular disease is the leading cause of mortality in people with diabetes. Diabetic individuals have a 2 to 4 fold increased risk for having cardiovascular events compared to patients without diabetes[22]. People with diabetes have a two to three fold greater morbidity and mortality following a myocardial infarction[23]. Although diabetic patients have a higher prevalence of traditional CAD risk factors such as hypertension, dyslipidemia and obesity when compared with people without diabetes, these risk factors account for less than half the excess mortality associated with diabetes. Thus, the diagnosis of diabetes is a major independent risk factor for the development of CAD and for adverse outcomes following a cardiovascular event.

Many therapies have been shown to be beneficial for reducing the cardiovascular events in people with diabetes such as treatment of hypertension and dyslipidemia and the use of aspirin, ACE inhibitors and ß blockers. However, early identification of patients with CAD is very essential for these therapies to be maximally effective in diabetic patients. Recognition of a previously undiagnosed myocardial infarction or knowledge of the presence of CAD will have an impact on the type and aggressiveness of therapy to be given. In patient with diabetes who had no symptoms of CAD, clinicians must decide when to initiate testing for CAD, and equally important, what testing algorithm is optimal.

CAD IN DIABETES

Most of the Type 2 DM patients frequently have many of the traditional CAD risk factors and usually present with CAD in the 5th or 6th decade of life or later, often after a relatively short period from diagnosis of diabetes, or even at diagnosis unlike type 1 DM patients.

Not infrequently, diabetes is first identified when the patient with CAD presents with angina, MI, or heart failure. The premature occurrence of CAD in diabetic patients, the more extensive coronary artery disease at the time of diagnosis, and the higher morbidity and mortality following MI are due to the more diffuse and distal involvement of coronary arteries in these patients[24].

CAD in diabetes is associated with generalized endothelial dysfunction and abnormalities of small vessels as well. Diabetic patients, more frequently have multiple coronary vessels involved by the time coronary artery disease is diagnosed or at the time of myocardial infarction. Diabetic patients are more prone for developing congestive heart failure because of the more diffuse coronary atherosclerotic process, particularly in the post myocardial infarction setting[25]. However, impaired ventricular function in diabetes is not only limited to the post-MI setting because impaired diastolic function has also been demonstrated in diabetic patients even in the absence of significant atherosclerotic CAD[26].

Acute coronary syndromes such as acute MI, unstable angina, and perhaps sudden death, commonly have luminal thrombus formation. Over time, increased thrombotic activity may accelerate the atherosclerotic process. The coagulation abnormalities associated with diabetes such as increased platelet aggregation and increased levels of fibrinogen and plasminogen activator inhibitor (PAI-1) may accelerate the development of coronary artery thrombosis. Increased platelet aggregation is related to the hyperglycemia of diabetes and insulin resistance. Hypertriglyceridemia and hyperinsulinemia which are frequently seen in diabetes may be related to the elevated levels of PAI-1[27].

The autonomic innervations of the heart can be affected in people with diabetes, which leads to a characteristic elevation in resting heart rate and decreased beat to beat variation. As autonomic dysfunction progresses, the heart rate response to posture or Valsalva manoeuvre and the circadian changes in blood pressure are both diminished. Symptomatic autonomic neuropathy increases the risk of sudden death in people with diabetes. Cardiovascular autonomic neuropathy occurs in ≈17% of patients with type 1 diabetes and ≈22% of those with type 2 DM[28]. Silent myocardial ischemia in diabetic patients is also contributed by cardiac autonomic neuropathy and this complicates the detection of CAD[29]. As a consequence, diabetic patients may be asymptomatic or

present with atypical symptoms such as easy fatigability, exertional dyspnoea, or indigestion.

BENEFITS OF EARLY DIAGNOSIS

The potential benefits of diagnosing asymptomatic CAD in patients with diabetes include

1) The early implementation of preventive programs aimed at reducing the risk of future coronary morbidity and mortality
2) The early initiation of anti-ischemic medications, and
3) The early identification of the patient for whom revascularization is appropriate.

Evidence from subgroup analysis of many secondary prevention trials enrolling diabetic patients with known CAD indicates that aggressive treatment can effectively reduce cardiovascular morbidity and mortality[30,31]. Although these results support the risk factor intervention in patients with diabetes and known CAD, similar data are lacking for a population of patients with asymptomatic coronary artery disease. Nevertheless, the increased morbidity and mortality from CAD in patients with diabetes provides a rationale for diagnostic evaluation in asymptomatic diabetic patients and aggressive "secondary" intervention when CAD is identified.

THE DESIGN OF PREVENTION PROGRAMS

The most compelling rationale at the present time for prompt diagnosis of coronary artery disease in patients with diabetes is the striking benefits observed in the lipid lowering trials. In the Scandinavian Simvastatin Survival Study (4S), cholesterol lowering was associated with a 42% reduction in cardiovascular mortality and a 30% reduction in total mortality in an overall group of 2,200 men and women with coronary disease, compared with placebo[30]. About 5% of the subjects had diabetes, and simvastatin treatment in that group was associated with a 55% reduction in major coronary events. In another study, the Cholesterol and Recurrent Events Trial (CARE)[31], where 14% of the participants had diabetes, a 25% reduction in CAD events was seen with pravastatin therapy in both the diabetic and non-diabetic patients. Thus, early diagnosis of asymptomatic CAD disease should encourage aggressive lipid lowering therapy. The National Cholesterol Education Program (NCEP) guidelines[32] and the recently published 2010 ADA recommendations for treating dyslipidemia[33] set different goals of therapy according to the absence or presence of coronary artery disease. This distinction suggests that the diagnosis of presymptomatic CAD should influence therapeutic decisions.

In patients with diabetes control of hypertension is so essential to reduce the onset and progression of diabetic nephropathy. The Joint

National Committee (JNC) 7 report recommends that patients with diabetes should be treated to reduce the blood pressure to a goal of < 130/80[34]. The presence of coronary artery disease or abnormal left ventricular function decides the choice of the selection of antihypertensive agent.

There are no well controlled studies to show that improved glucose control will reduce cardiovascular disease in patients with diabetes. However, in the Diabetes Control and Complications Trial (DCCT)[35], the intensive treatment group had a trend toward fewer cardiovascular events, although the number of actual events in this relatively young group of individuals was very low, and the effect of treatment did not reach statistical significance. In the Diabetes Mellitus Insulin Glucose Infusion in Acute Myocardial Infarction (DIGAMI) Study[36], hospital use of insulin glucose infusion, followed by 3 months of intensive insulin therapy in patients with acute MI, was associated with a 29% reduction in cardiovascular mortality after 1 year. Similarly in UKPDS Study the author found that the only macrovascular end point that demonstrated a trend in risk reduction in the main analysis was myocardial infarction (MI) (16% risk reduction), but did not quite reach statistical significance[37].From these studies we can understand that aggressive glycemic control will be another approach to the prevention of cardiac events but more studies will be needed to assess its real significance.

The efficacy of aspirin therapy in reducing CAD has been studied extensively. The diabetic subjects included in the Meta analysis of 145 prospective studies of aspirin use conducted by the Anti-Platelet Trialists[38] had reductions in MI, stroke, transient ischemic episodes, or development of signs and symptoms of coronary disease similar to non-diabetic subjects. In the Early Treatment Diabetic Retinopathy Study (ETDRS)[39], diabetic patients without pre existing coronary artery disease who received aspirin had a 15% reduction in the incidence of first MI over a 7-year period. In that study, diabetic patients with pre existing CAD also benefited. In a sub-group analysis of the Physicians Health Study [40], diabetic physicians receiving aspirin for primary prevention had a reduced relative risk of MI. These data have led the ADA to recommend the consideration of aspirin therapy for primary prevention in those with diabetes at increased cardiovascular risk that includes men >50 years of age or women >60 years of age with at least one additional major risk factor and the use of aspirin therapy as a secondary prevention strategy in men and women with evidence of large vessel disease[41].

ACE inhibitors are recommended as the first line treatment of hypertension in diabetes and in diabetic patients with proteinuria[42]. However, the demonstration of coronary artery disease, and identification of left ventricular dysfunction, would also be a strong indicator for ACE inhibitor treatment in the normotensive, non proteinuric patient.

INITIATION OF ANTI-ISCHEMIC THERAPY

In patients with diabetes who have had an MI, ß blocker treatment is very important to reduce the mortality. So, the diagnosis of a previously unrecognized MI in these patients is critical in the management. In the Bezafibrate Infarction Prevention Study[43], patients treated with ß-blockers had an approximately 50% reduction in mortality, compared with those patients not receiving that treatment. ß Blocker therapy was also effective in the DIGAMI Study[36]. Also, the use of cardioselective ß blockers is particularly beneficial in diabetic patients with reduced heart rate variability.

REFERRAL FOR REVASCULARIZATION

Testing for asymptomatic coronary disease may help identify patients with severe coronary obstruction in whom revascularization should be considered, although the benefit of percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft (CABG) in people with asymptomatic CAD and diabetes is not clear. The Bypass Angioplasty Revascularization Investigation (BARI) trial[44] indicated excellent 5-year survival in symptomatic diabetic patients with advanced multi-vessel coronary disease treated with CABG. In the same study, selected patients who received an internal mammary artery graft, cardiac mortality was 2.9% at 5 years. On the other hand, the BARI trial raised serious concern for the use of PTCA in multi-vessel disease, since

diabetic patients randomized to PTCA had a greatly increased 5-year mortality (35% overall and 20% cardiac) compared with patients randomized to CABG with or without an internal mammary artery graft (19% overall and 6% cardiac). Subgroup analyses of the Emory Angioplasty versus Surgery Trial (EAST)[45] and the Coronary Angioplasty versus Bypass Revascularization (CABRI)[46] trials showed that CABG tended to be associated with better long-term survival over balloon only PCI for 3-vessel disease

Although nonrandomized patients in the BARI registry and other patients in observational studies with multi-vessel disease have shown a higher survival rate when treated with PTCA, there still remains concern for the use of multi-vessel PTCA to improve the prognosis in asymptomatic patients with diabetes. The higher restenosis rate associated with PTCA in diabetic patients (up to 63%)[47] also limits the use of routine balloon angioplasty for asymptomatic patients with single-vessel disease.

ROLE OF CARDIAC TESTING

People with diabetes may present for evaluation with an established CAD history or for having a prior cardiac event, in which case they warrant testing for risk stratification. However, the challenge faced by the physician caring for a patient with diabetes is to accurately identify patients without a prior history of a cardiovascular event and patients not

manifesting the symptoms strongly suggesting CAD, in whom additional testing is indicated.

There are no evidence based guidelines for screening asymptomatic diabetic patients for coronary artery disease (CAD). One well studied screening tool is exercise treadmill testing. Many diabetic patients with no symptoms of CAD have abnormal stress tests. For asymptomatic patients, identification of cardiovascular risk factors and risk stratification may help physicians justify the performance of treadmill evaluation. Patients considering moderate or vigorous exercise and those at highest risk can undergo exercise stress testing with referral for further evaluation as indicated. For patients with decreased exercise capacity, inability to reach target heart rates, or absence of chest pain during exercise, stress nuclear imaging may be more valuable than exercise electrocardiograph testing. In general, the test chosen will depend on the purpose of the test.

The American Heart Association Prevention VI Conference[48] emphasized that there are no outcome data to support stress testing in asymptomatic diabetic patients.

INDICATIONS FOR STRESS TESTING IN DIABETIC PATIENTS

The ADA[49] advocates for stress testing in diabetic patients with

1. Typical or atypical cardiac symptoms
2. Resting electrocardiograph suggestive of ischemia or infarction
3. Peripheral or carotid occlusive arterial disease

4. Sedentary lifestyle, age >35 years, and planning to begin a vigorous exercise program
5. Two or more of the following risk factors in addition to diabetes
    - Total cholesterol ≥240 mg/dl, LDL cholesterol ≥160 mg/dl, or HDL cholesterol ≤35 mg/dl
    - Blood pressure ≥140/90 mmHg
    - Smoking
    - Family history of premature CAD
    - Positive micro/macro albuminuria test.

Ambulatory monitoring of ST segment changes

Chiariello et al[50] compared the incidence of ambulatory ischemia during 24-hour AECG monitoring among 51 patients with diabetes (74% of whom had evidence of coronary disease), 70 nondiabetic patients with coronary disease, and 40 nondiabetic patients without overt coronary disease. They reported that 36% of the diabetic patients had at least one episode of asymptomatic ischemia, significantly higher than the 17% of patients in the nondiabetic group with coronary disease. Additionally, 73% of the total episodes of ST-segment deviation in the diabetic group were asymptomatic, significantly higher than the 60% of episodes in the nondiabetic group.

In the Asymptomatic Cardiac Ischemia Pilot (ACIP)[51], ≈90% of patients had only asymptomatic ST-segment depression during the

qualifying 48-hour AECG recording. There was no difference in the prevalence of asymptomatic ST-segment depression in the diabetic and nondiabetic ACIP groups

In general, the utility of ambulatory monitoring of electrocardiographic ST-segment changes to detect coronary disease in asymptomatic populations has been disappointing and not cost effective.

Coronary artery calcification:

The coronary calcium score is an excellent marker for the overall coronary atherosclerotic burden and identifies asymptomatic individuals at higher risk for inducible ischemia. If in the judgment of the clinician an asymptomatic patient is a candidate for CAD testing, it is reasonable to apply cardiac CT for detection of coronary artery calcification, using either electron beam or multislice technology, as the first step. The calcium score may also identify those at risk of subsequent coronary events but should be used with full knowledge of the patient's complete cardiovascular risk profile.

The American Heart Association scientific statement[52] states that coronary calcium testing is not valuable in individuals at low Framingham risk but may be useful as a screening tool in those at intermediate risk, which would include patients with diabetes. However, there was only limited support for coronary calcium testing of patients at intermediate risk, with a class IIb recommendation (level of evidence B).

Moreover, the American College of Cardiology appropriateness criteria for cardiac CT[53] indicates that the usefulness of screening asymptomatic intermediate risk populations with this technology is currently unknown[54]. Anand et al.[55] studied asymptomatic patients with diabetes and confirmed the higher incidence of inducible ischemia in patients with higher calcium scores. If coronary calcium testing is performed, it appears reasonable to proceed with further testing in diabetic patients with calcium scores >400, considering factors such as age and renal function. The higher cost of the investigation precludes its availability to the general population.

Exercise electrocardiography

Exercise ECG testing remains a well established, inexpensive test available to assist clinicians in the diagnosis and prognosis of CAD in diabetic patients. It appears to have similar diagnostic sensitivity (≈50%) and specificity (≈80%) for diabetic patients presenting with angina as for non-diabetic patients[56]. It can identify a subgroup of asymptomatic diabetic patients who have significant CAD as defined by angiography, and in lower risk diabetic cohorts, it may offer short term prognostic reassurance to those asymptomatic patients with negative tests. However, considerable prognostic power of the exercise ECG test lies beyond the ST-segment response and the presence of angina during exercise.

Parameters including exercise capacity and HRR (Heart Rate Recovery) offer significant information, particularly in diabetic patients, who may not experience angina during exercise and who may have increased autonomic dysfunction. P Michael Ho et al[57] showed that impaired chronotropic response to exercise stress testing in patients with diabetes predicts future cardiovascular events. Further studies are needed to assess the value of these non ST segment variables among patients with DM.

Stress perfusion imaging

This investigation requires the effort on the patient side to walk. In elderly patients who have associated osteoarthritis, this may be a difficult investigation to perform.

Stress nuclear testing has a sensitivity of 88% and specificity of 74% for the detection of angiographic CAD in the general clinical population and has been found to have similar diagnostic value among diabetic cohorts[58]. Stress nuclear testing appears to be useful in risk stratification among higher risk asymptomatic diabetic patients.

In the largest series reported, Rajagopalan and colleagues[59] assessed the prognostic implications of stress nuclear testing in their cohort of 1427 asymptomatic diabetic patients. When patients were stratified by their stress nuclear test results into low, medium, and high risk groups, the authors found a significant difference among annual

mortality rates (3.6%, 5.0%, and 5.9% respectively) . De Lorenzo et al[60] reported that among 180 asymptomatic diabetic patients who underwent exercise or dipyridamole nuclear stress testing, 26% had abnormal SPECT imaging. Death or MI occurred in 3% of those with no perfusion defects, 10% of those with perfusion defect in a single territory, and 31% of those with perfusion defects that involved more than 1 territory.

In summary, perfusion imaging is useful in patients with diabetes since the technique provides quantifiable data and identifies low and high risk patients for future adverse cardiovascular events. However, the expertise and technical requirements required for performing nuclear testing is not widely available in India and is beyond the reach of the common man.

Stress echocardiography

Stress echocardiography has a mean sensitivity of 86% and a specificity of 81% in the general population[61]. Hennessy et al[62] evaluated 52 patients with DM referred for cardiac assessment using dobutamine stress echocardiography (DSE). Sensitivity, specificity, and positive and negative predictive values of DSE for CAD detection were 82%, 54%, 84%, and 50%, respectively.

Penfornis et al[63] compared the efficacy of DSE to exercise ECG testing and SPECT (Single Photon Emission Computed Tomography) nuclear perfusion imaging in 56 asymptomatic diabetic patients with 3

additional cardiovascular risk factors but normal resting ECGs. Participants underwent all forms of non-invasive stress testing, but coronary angiography was only performed if at least 1 test was abnormal (47%), which precluded the measurement of diagnostic sensitivity and specificity. Positive predictive value was 69% for DSE, 60% for exercise ECG and 75% for thallium SPECT.

Stress echocardiographic imaging provides improved sensitivity and specificity compared with exercise ECG testing. Increasing data are available to support both its diagnostic accuracy and in particular, its prognostic ability to risk stratify diabetic patients for future cardiac events

ANLKLE BRACHIAL INDEX

There are several established procedures for estimating subclinical atherosclerotic changes in human arteries. Increased carotid intima media thickness (IMT) is associated with future cerebrovascular and cardiovascular events[64,65]. Pulse wave velocity is related to arterial wall stiffness, future hypertension and cardiovascular diseases[66,67]. Coronary artery calcium screening is the another method for evaluating the CVD risk in asymptomatic patients[68-70]. All these methods, however, require sophisticated equipment and a specialized user. Accordingly, they are not well suitable for the screening of early arterial changes in a routine office practice and there is a great need for a simple non invasive tool that could

be used in an office setting to screen for arterial stiffness or subclinical atherosclerosis such as ankle brachial index (ABI)

The ankle blood pressure is usually measured in conjunction with the arm blood pressure and the ankle brachial pressure index (ABI) is calculated. Decreased ABI is strongly associated with cardiovascular diseases[71-80]. Also an elevated ABI value seems to be a significant risk factor of CVD[81,82]. The ankle brachial index (ABI) is widely accepted as a diagnostic test used to evaluate the presence of lower extremity peripheral artery disease (PAD) in patients with symptoms of intermittent claudication or rest ischemia[83-85]. However, the majority of patients with PAD are asymptomatic and therefore, measurement of the ABI only when prompted by symptoms will result in most cases of PAD going unrecognized[86].

The measurement of the ABI in patients without symptoms of PAD is controversial. In 2005, the United States Preventive Services Task Force assigned a "D" recommendation to screening for PAD, a grade indicating minimal benefit and possible harm[87]. This recommendation was based on evaluation of limb outcomes such as claudication, amputation, and impaired ambulation. However, most patients with PAD do not go on to have major adverse limb outcomes. They do, however, have an excessively high burden of cardiovascular morbidity and mortality. Diehmand et al[88,89] make an important contribution to the

mounting evidence that screening for PAD in asymptomatic individuals should be considered in terms of cardiovascular and not limb outcomes.

In the German Epidemiological Study on Ankle Brachial Index (getABI)[90], a prospective observational cohort study on the prognosis of elderly (aged >65 years) individuals with a low ABI compared with those with a normal ABI, they reported that 21% of subjects screened had PAD and the presence of PAD was associated with a 2-fold adjusted risk of death or severe cardiovascular events. In persons with PAD, the risk of a severe coronary vascular event was 3-fold that of a peripheral vascular event. Their findings reinforce the concept that the measurement of the ABI as a part of primary care practice would identify a significant number of persons at heightened risk for cardiovascular morbidity and mortality and that limb events are infrequent relative to total cardiovascular events in patients with PAD. Thus, the greatest relevance of the ABI may not be for the limb but rather as a biomarker of cardiovascular risk.

THE ABI AS A BIOMARKER OF CARDIOVASCULAR RISK:

A National Institutes of Health working group defined a biomarker as "a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacological responses to a therapeutic intervention"[91].The ABI

meets this definition as an objectively measured indicator of a pathogenic process.

It measures a specific pathology (i.e., systemic atherosclerosis) because the cumulative prevalence of non-atherosclerotic causes of a low ABI (eg. giant cell arteritis) is very low. It adds to clinical assessment because the history and physical examination are often insufficient to correctly diagnose or rule out PAD[92]. The ABI is acceptable to the patient because it causes only mild discomfort and poses no risk such as radiation exposure. Most often, a single measure is sufficient to diagnose PAD[85]. It is applicable to men and women of all ages and has been tested in numerous ethnicities. The measurement is standardized, and it is both accurate and precise. The ABI has known reference limits; an ABI $\leq$0.90 has been validated as both a sensitive and a specific marker of PAD. Its specificity is not only for the presence of PAD but also for adverse cardiovascular outcomes, making it unlikely to mislabel or harm asymptomatic individuals[93]. It has been tested in healthy individuals as well as in persons with varying severity of cardiovascular disease. The measurement takes only a few minutes, it does not require specialized equipment or a specialized technician, and has immediate turn around. A previous report from the getABI group demonstrated that the ABI determination is highly reproducible and reliable when done in a primary care setting by physicians and non-physicians with little training[94].

There is a consistent series of prospective epidemiological studies indicating that an abnormal ABI predicts cardiovascular disease. A systematic review and meta-analysis including 7 population based studies with a total of 28,679 subjects found a consistent relationship between a low ABI and an adverse cardiovascular prognosis. The specificity of low ABI for coronary heart disease, stroke, and cardiovascular mortality was 92.7%, 92.2%, and87.9%, respectively. The adjusted relative risk for cardiovascular mortality ranged from 2.0 to 6.3[93].

A patient level meta analysis (ABI Collaboration) highlights that a low ABI predicts cardiovascular disease in those without a history of coronary heart disease[95]. In this analysis of 16 studies including 48,294 individuals, a low ABI conferred an adjusted relative risk for cardiovascular mortality of 2.9 in men and 3.0 in women. Diehm et al found that PAD was associated with an adjusted relative risk for cardiovascular mortality of 2.1, consistent with the results of these meta-analyses[95]. A final important aspect of the ABI as a cardiovascular disease biomarker is that it adds to the ability to predict risk over and above that already achievable through the use of established cardiovascular risk factors. The ABI Collaboration found that including the ABI in addition to the widely used Framingham Risk Score reclassified 19% of men and36% of women into a different category of risk[95].

Diehm et al[88,89] did not test whether PAD reclassified patient risk, although they did demonstrate that the association of PAD with incident cardiovascular disease was independent of cardiovascular risk factors. In fact, the presence of PAD was the strongest predictor of death or severe vascular events in a fully adjusted multivariable model.

PAD IN PEOPLE WITH DIABETES

Peripheral arterial disease (PAD) is a frequent manifestation of atherosclerosis in the general population and is two to four times more prevalent in diabetic patients[96]. A continuous wave Doppler measured ankle brachial index (ABI) ≤0.90 is commonly used for diagnosing PAD[83,86]. Ankle brachial index (ABI) sensitivity is 79% and specificity is 96% for detection of ≥50% reduction in vascular lumina[97]. Moreover, ABI has prognostic value for cardiovascular morbidity and mortality and for coronary artery disease in particular[98].

The ADA consensus panel states that PAD in people with diabetes is different from the vascular disease due to other risk factors in its biology, in its clinical presentation, and in its management. As far as the prevalence and impact are concerned, diabetes is the most powerful risk factor for PAD. Among those with diabetes, age, duration of diabetes, and the presence of neuropathy are particularly important as risk factors for the development of PAD[99].

With diabetes, there is usually a unique involvement of the tibial vessels below the knee. Because of the pattern of involvement distally, the majority of patients lack classic symptoms, such as claudication. In addition, there is an almost invariable association with neuropathy with blunted pain perception. Patients are therefore likely to experience more subtle symptoms (fatigue or poor functioning) than with classic claudication. A more devastating consequence of neuropathy is that PAD patients with diabetes present late, having already developed limb threatening ischemia with tissue loss, gangrene, or rest pain. This unfortunate progression lends urgency to the task of uncovering PAD in asymptomatic individuals in order to prevent amputation. Beyond the threat to the limb, these patients face enormous cardiovascular and cerebrovascular risk.

Over 5 years, 20% of PAD patients will sustain nonfatal myocardial infarction or stroke, and 30% will die, largely from cardiovascular disease[100]. For those with critical limb ischemia, the prognosis is worse: 30% will have amputations, and 20% will die within 6 months[86]. The true prevalence of PAD in individuals with diabetes has been difficult to determine because of the lack of symptoms and insensitive means of diagnosis. Using the ABI, a study done by Elhadd et al found that the prevalence of PAD in individuals with diabetes > 40 years of age was around 20%[100,101].That figure is higher than would be

anticipated using only symptoms and absent pulses. In PAD patients > 50 years of age, the diabetes prevalence was 29%, again higher than anticipated[102].The unexpectedly very high prevalence of Peripheral Artery Disease in the population with diabetes in a sense makes PAD a new public health issue.

It is important for clinicians to assess patients for PAD to identify those with high cardiovascular risk and those at risk for amputation. Because of the lack of symptoms in the premorbid period, it is important to screen those at risk. The ADA consensus statement recommends screening for PAD in anyone with diabetes over 50 years of age. Those with other risk factors (e.g., smoking, advanced age, hypertension, and hyperlipidemia) or a duration of diabetes > 10years should also be screened[103].

Measurement of ABI is more reliable and more specific than what can be learned from the history and physical exam. Medial arterial calcification can make arteries at the ankle poorly compressible, giving a false elevation of the ABI, typically > 1.3. Such false negatives are not common enough, however, to detract from the value of the ABI as a screening tool. If one suspects non-compressible vessels, then more detailed evaluation with toe pressure or pulse volume recordings would be indicated.

Finally, it should be noted that ABI screening for PAD in patients with diabetes is enormously productive. As noted above, routine screening of individuals over 50 years of age can be expected to identify PAD in nearly one-third of individuals. Furthermore, identifying PAD before it has progressed to its more severe stages in this population allows us to offer effective treatments. These therapies may arrest PAD development and perhaps, as we have seen with regression of atherosclerosis through aggressive blood pressure and lipid control, reverse its advance. At the same time, we will undoubtedly be reducing cardiovascular risk.

MATERIALS AND METHODS

MATERIALS

The present study was a cross sectional study carried out between May and November 2011 on patients who were admitted to the Rajiv Gandhi Government General Hospital, Chennai, a tertiary care referral hospital in Tamilnadu. The protocol of the study was approved by the Institutional Ethics Committee, Madras Medical College, Chennai-600003 and detailed informed written consent was obtained prior to enrolment in the study from the patient.

STUDY POPULATION

One hundred (100) patients admitted to the various medical wards and attending the outpatient clinics of Rajiv Gandhi Government General Hospital, Chennai were enrolled for the present study.

INCLUSION CRITERIA

Patients with type 2 DM without established cardiovascular symptoms and disease (as per the records available with them)

EXCLUSION CRITERIA

- Patients with type 2 DM with previous history of established cardiovascular disease.(as per the records available with them)
- Patients with type 2 DM with cardiac symptoms (angina and angina equivalents)
- All type 1 DM patients

- Patients with established/clinically manifested calcification of peripheral arteries
- Patients with vasculitis
- Patients with type 2 DM with established PAD in the form of gangrene and amputation in legs.

METHODS

- Each patient was interviewed to obtain detailed history and examined thoroughly including all peripheral pulses and bruit.
- Height, weight and waist circumferences were measured with standardized techniques and equipments in all patients. Waist Circumference measured at midpoint between the costal margin and anterior superior iliac spine. Hip Measurement taken as maximum diameter at the greater trochanter.
- BMI and Waist hip ratios were computed in all patients.

  BMI calculated based on the Quetelet formula by dividing weight (in kg) by the square of height (in m^2).

  BMI was taken as <18.5 - underweight, 18.5-22.9 - normal, 23-24.9 - overweight, >25 - obese.

  WHR - > 0.85 – was taken as abnormal value in female. > 0.90 in male as abnormal value.

- Blood pressure was measured in sitting position in the right upper limb in all patients. Patients were considered as hypertensive if blood pressure was > 130/80 mm Hg or patients already on antihypertensive therapy.
- Serum total cholesterol, triglycerides, HDL, LDL estimation were done after 12 hours of fasting in all patients.

  Dyslipidemia was taken as total cholesterol >200mg/dl or triglycerides >150mg/dl or LDL >130mg/dl or HDL <40 (males), < 50 (females)
- Fasting and post prandial blood sugar, HbA1c, serum creatinine were done in all patients.

  Fasting blood sugar measured after 8 hours of overnight fasting and post prandial blood sugar measured 2 hours after the meals.

  Fasting Hyperglycemia means if Blood glucose value ≥126 mg/dl and Post prandial hyperglycemia means if value ≥200 mg/dl.

  HbA1c <7 was taken as under good glycemic control and HbA1c ≥7 was taken as not in good glycemic control.
- ECG and Echocardiographic evaluation were done to rule out the presence of previous heart disease.

TREADMILL TEST

Treadmill test was done for all patients in Department of Cardiology following the BRUCE protocol under the supervision of a well experienced cardiologist.

Patient Preparation

- Patients were instructed not to eat or smoke for 3 hours before the test and should be dressed appropriately for exercise, especially with regard to footwear. No unusual physical efforts should be performed for at least 12 hours before testing.
- Drugs such as ß blockers or nitrates were withdrawn 24 hours prior to testing as it may attenuate the exercise responses and limit the test interpretation.
- A brief history and physical examination were done to rule out any contraindications.
- A resting standard 12-lead electrocardiogram (ECG) was obtained to rule out any differences from the resting pre-exercise ECG.
- Standing ECG and blood pressure were recorded to determine vasoregulatory abnormalities and positional changes, especially ST-segment depression.
- A detailed explanation of the testing procedure was given to the patient which outlines risks and possible complications. The

patients were instructed on how to perform the test with demonstration by the investigator.

BRUCE PROTOCOL[104]

The Bruce protocol is very widely used and has been extensively validated. There are 7 stages of 3 minutes each so that a complete test takes 21 minutes. First stage starts at a speed of 1.7 miles per hour (mph) and a gradient of 10%. Each subsequent stage has an increment of 0.7 to 0.8 mph in speed and 2% in gradient. The level of exercise is estimated in METs where 1 MET (metabolic equivalent) is the amount of energy expended at rest or 3.5 ml oxygen per kilogram per minute.This can be better explained with the help of the following table.

Bruce Protocol

Stage	Minutes	% grade	km/h	MPH	METS
1	3	10	2.7	1.7	4.7
2	6	12	4.0	2.5	7.0
3	9	14	5.4	3.4	10.1
4	12	16	6.7	4.2	12.9
5	15	18	8.0	5.0	15.0
6	18	20	8.8	5.5	16.9
7	21	22	9.6	6.0	19.1

MPH - miles per hour, METS – metabolic equivalents

An adequate test is performed if the patient can achieve 85% of their maximum heart rate (calculated as 220-age in years for men and 210-age for women).

The modified Bruce protocol has two 3-minute warm up stages at 1.7 mph and 0% grade and 1.7 mph and 5% grade, and it is used in older individuals and those whose exercise capacity is limited (post MI)

Exercise Test Supervision

Exercise testing was conducted by well trained personnel with a sufficient knowledge of exercise physiology and equipments, medications, and personnel trained to provide advanced cardiopulmonary resuscitation (CPR) was readily available.

Exercise Test Interpretation

Interpretation of the test was done by well experienced cardiologist in department of Cardiology by taking exercise capacity and clinical, hemodynamic, and ECG responses into consideration. Exercise testing was terminated by following the indications given by ACC/AHA[104].

Indications for Terminating Exercise Testing:

Absolute Indications

- ST-segment elevation (>1.0 mm) in leads without Q waves (other than V1 or aVR).
- Drop in systolic blood pressure >10 mm Hg (persistently below baseline), despite an increase in workload, when accompanied by any other evidence of ischemia.
- Moderate-to-severe angina (grade 3 to 4)

- Central nervous system symptoms (eg. ataxia, dizziness, or near syncope).
- Signs of poor perfusion (cyanosis or pallor).
- Sustained ventricular tachycardia.
- Technical difficulties monitoring the ECG or systolic blood pressure.
- Subject's request to stop.

Relative Indications

- ST or QRS changes such as excessive ST displacement (horizontal or down-sloping of >2 mm) or marked axis shift.
- Drop in systolic blood pressure >10 mm Hg (persistently below baseline) despite an increase in workload, in the absence of other evidence of ischemia.
- Increasing chest pain.
- Fatigue, shortness of breath, wheezing, leg cramps, or claudication.
- Arrhythmias other than sustained ventricular tachycardia, including multifocal ectopic, ventricular triplets, supraventricular tachycardia, heart block, or bradyarrhythmias.
- General appearance.
- Hypertensive response (systolic blood pressure >250 mm Hg and/or diastolic blood pressure >115 mm Hg).
- Development of bundle-branch block that cannot be distinguished from ventricular tachycardia.

ANKLE BRACHIAL INDEX

All ABI were measured in a temperature controlled room (24° ± 1 °C) where each subject rested supine for 5 minutes before measurements were started. ABI was measured by an examiner with experience in ABI measurement and who was blinded to all clinical baseline parameters.

Doppler assisted ABI measurements were performed according to the method described by Lovelace and Moneta[105] using a sphygmomanometer with a cuff width ranging between 29 and 40 cm and a Doppler device with an 8.2 MHz continuous wave probe.

An appropriate sized blood pressure cuff was placed on the arm with the limb at the level of the heart. Ultrasound gel was placed over the patient's brachial pulse. Transducer of the handheld Doppler was placed on the gel and the position of the transducer was adjusted till the maximum intensity of the signal was obtained. The cuff was inflated to about 20mmHg above the expected systolic BP of the patient till the doppler signal was disappeared. Then the cuff was slowly deflated approximately 1mmHg/sec until the Doppler signal re-appears. This was taken as the brachial systolic pressure. Similarly brachial systolic BP was measured in other upper limb.

In lower limbs, an appropriate sized blood pressure cuff was applied immediately proximal to the medial malleoli. The ultrasound gel was placed on the skin overlying the dorsalis pedis (DP) and posterior tibial (PT) arteries in the foot. Transducer of the handheld Doppler was placed on the gel and the position of the transducer was adjusted till the maximum intensity of the signal was obtained. Then the cuff was slowly inflated till no longer the signal was heard. Then the cuff was deflated using the same technique used in the arms until the Doppler signal re-

appears. This measurement was taken as systolic BP in DP of that limb. Similarly the systolic pressure of the PT was obtained. The same was repeated on the opposite leg.

Calculated ABI values were adjusted to 2 decimal places.

The diagnostic criteria for PAD[106] based on the ABI are interpreted as follows:

- Normal if 0.91–1.30
- Mild obstruction if 0.70–0.90
- Moderate obstruction if 0.40–0.69
- Severe obstruction if < 0.40
- Poorly compressible if > 1.30

STATISTICAL ANALYSIS

The data collected from the patients were entered in to the master chart prepared. The statistical analysis was done using GRAPH PAD PRISM version 5.0. For non-parametric data, Fisher's exact test was used. For parametric data, student's t-test or ANOVA (ANalysis of One way VAriance) was done as deemed appropriate to the data of interest. The significance of the statistical test was graded as * – significant ($p < 0.05$), ** – very significant ($p<0.01$), *** – highly significant ($p<0.001$), **** – very highly significant ($p<0.0001$), # – not significant.

OBSERVATIONS AND ANALYSIS

AGE DISTRIBUTION

Age of the 100 patients selected for the study ranges from 37 to 60 years.

TABLE 1: AGE DISTRIBUTION

AGE OF PATIENT	NO. OF PATIENTS
31-40	9
41-50	40
51-60	51

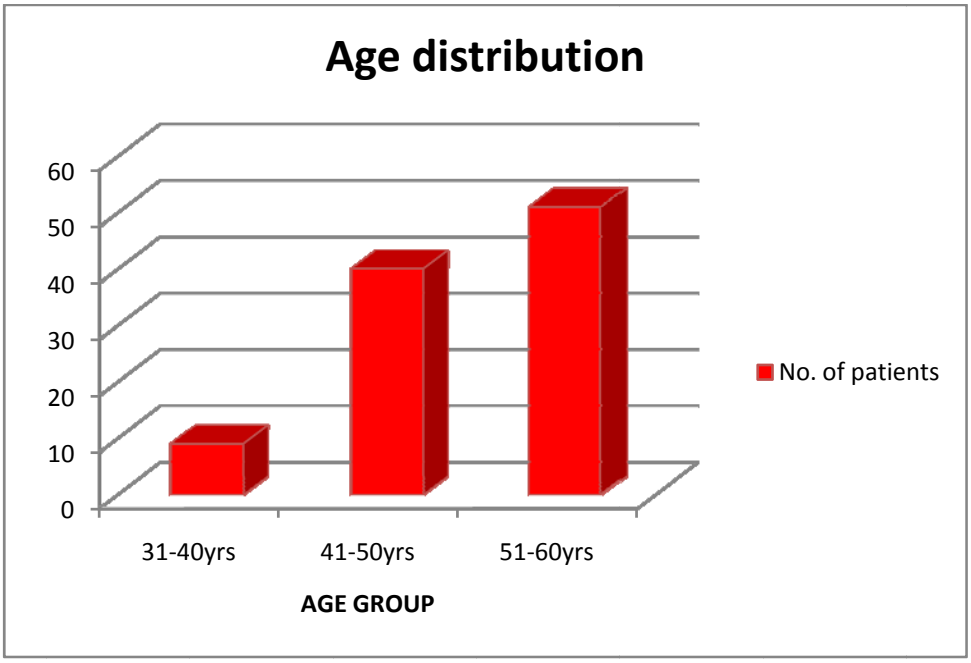
GENDER DISTRIBUTION

Gender distribution of the 100 patients selected randomly for the study 56 were males and the remaining 44 were females.

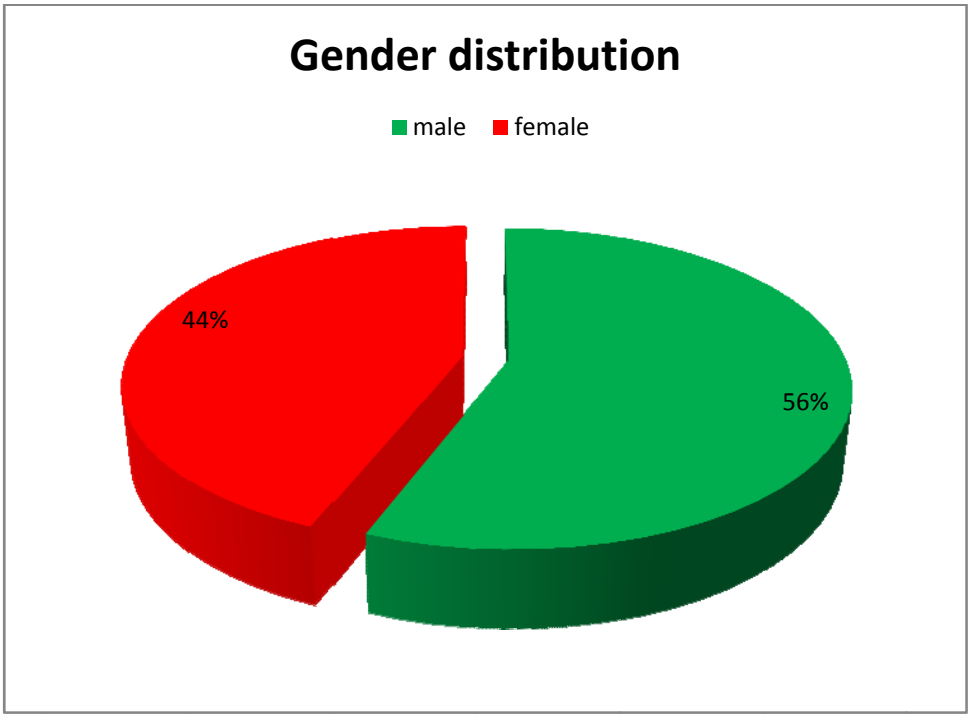
TABLE 2 : GENDER DISTRIBUTION

SEX	NO. OF PATIENTS
MALE	56
FEMALE	44

GRAPH 1 : DISTRIBUTION OF AGE



GRAPH 2 : GENDER DISTRIBUTION



SHT

Among the 100 patients studies 43 had hypertension. Majority of the hypertensive were males 26(60.47%). Largest number of hypertensive 25 (58.14%) were in the 50-60 years age group.

TABLE 3 : SHT AND SMI

	NO SMI		**YES SMI**	
	NO	**%**	**NO**	**%**
NORMOTENSIVES	51	61.45	6	35.29
HYPERTENSIVES	32	38.55	11	64.11
TOTAL	83		17	
P VALUE	0.0613#			

There was no statistically significant correlation between hypertension and SMI.

ACTIVE SMOKER

None of the females were active smokers. Out of the 56 males 34 (60.71%) were active smokers.

TABLE 4: SMOKING AND SMI

	NO SMI		YES SMI	
	NO	**%**	**NO**	**%**
NONSMOKER	56	67.47	10	58.82
SMOKER	27	32.53	7	41.18
TOTAL	83		17	
P VALUE	0.5768#			

No significant correlation between smoking and SMI.

ALCOHOLIC

Among the 100 patients studied only male alcoholics were found. Out of the 56 males 35 (62.5%) were alcoholics.

TABLE 5: ALCOHOL AND SMI

	NO SMI		SMI	
	NO	**%**	**NO**	**%**
NON ALCOHOLIC	53	63.86	12	70.59
ALCOHOLIC	30	36.15	5	29.41
TOTAL	83		17	
P VALUE	0.7815#			

No significant correlation between alcohol and SMI.

BMI

AGE AND BMI

Among the 100 patients studied 49 of them belongs to overweight and obese category and 51 of them belongs to normal and underweight category.

As age increases there is no significant increase in BMI and majority 31(60.78%) of the 51-60 years age group were normal and underweight.

TABLE 6: AGE AND BMI

AGE GROUP	BMI							
	UNDER WEIGHT		NORMAL		OVER WEIGHT		OBESE	
	NO	%	NO	%	NO	%	NO	%
31-40	0	0	2	5	4	14.29	3	14.29
41-50	4	36.36	14	35	14	50	8	38.09
51-60	7	63.67	24	60	10	35.71	10	47.62
TOTAL	11	100	40	100	28	100	21	100
MEAN	17.14		21.07		24.03		28.69	
S.D.	1.04		1.37		0.56		5.25	
P VALUE	1 #							

No statistically significant correlation between age and BMI.

SEX AND BMI

Among the 56 males in my study 30(53.57%) belongs to normal and underweight category and the remaining 26 (46.43%) belongs to overweight and obese category.

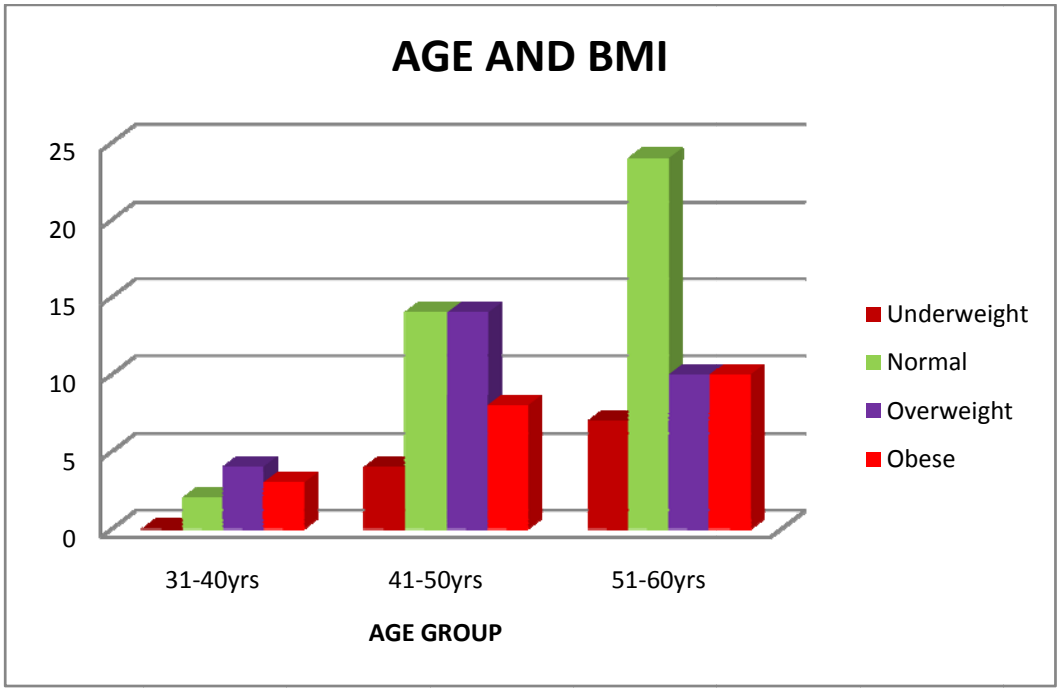
Among the 44 females i have studied 23 (52.27%) belongs to overweight and obese category and the remaining 21 (47.73%) belongs to normal and underweight category.

There was a slight increase in BMI among females compared to males but this difference was not significant statistically.

TABLE 7 : SEX AND BMI

SEX	BMI							
	UNDER WEIGHT		NORMAL		OVER WEIGHT		OBESE	
	NO	%	NO	%	NO	%	NO	%
MALES (56)	10	17.86	20	35.71	15	26.79	11	19.64
FEMALES(44)	1	2.27	20	45.45	13	29.55	10	22.73
P VALUE	0.6873#							

GRAPH 3 : AGE AND BMI



GRAPH 4 : SEX AND BMI

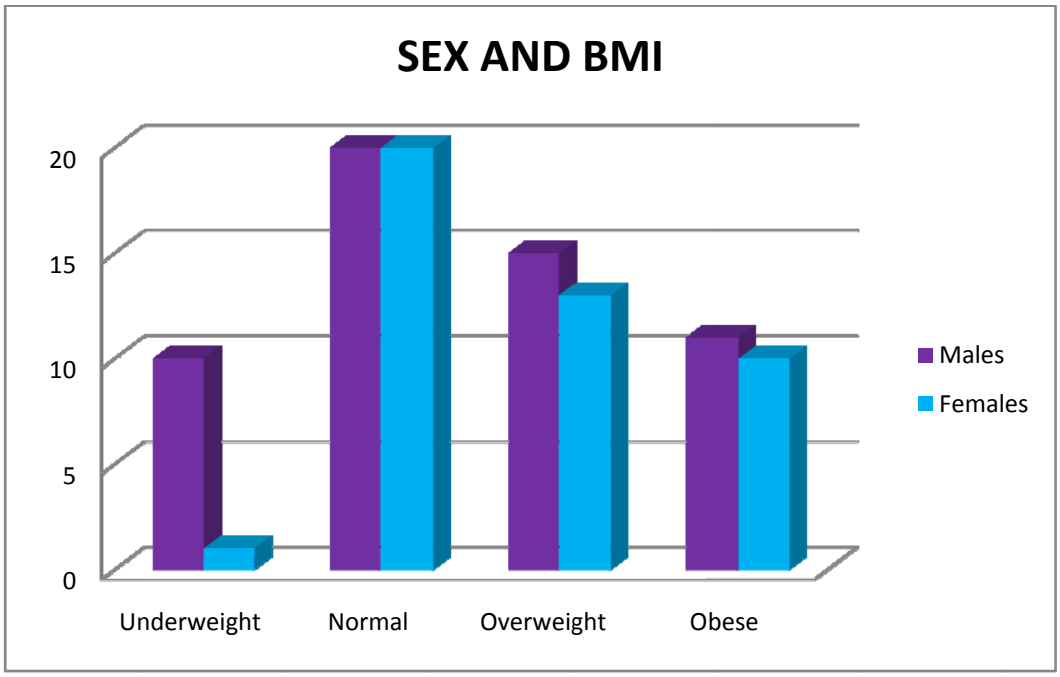


TABLE 8: BMI ANS SMI

BMI	NO SMI	YES SMI
MEAN±S.D	22.56±0.3841	25.52±1.664
P VALUE	<0.0100**	

There was a statistically significant correlation between BMI AND SMI.

W/H RATIO

SEX AND W/H RATIO

Among the 44 females 37 (84.09%) were having high W/H ratio and only 36 (64.29%) out of the 56 males were having high W/H ratio. Females having high W/H ratio compared to males.

TABLE 9 : SEX AND W/H RATIO

SEX	WAIST HIP RATIO			
	NORMAL		HIGH	
	NO	%	NO	%
MALES (56)	20	35.71	36	64.29
FEMALES (44)	7	15.91	37	84.09
P VALUE	0.0402*			

There is a stasitically significant relationship between sex and BMI.

GRAPH 5 : SEX AND W/H RATIO

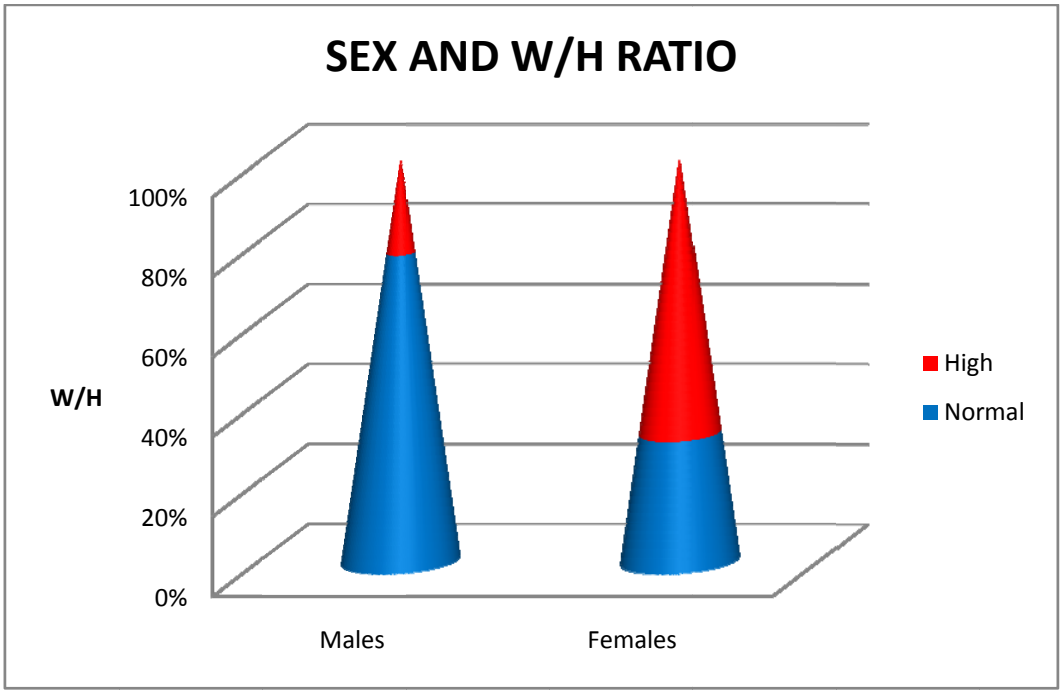


TABLE 10 : W/H RATIO AND SMI

W/H RATIO	NO SMI	YES SMI
MEAN±S.D.	0.8917±0.07	0.8882±0.01
P VALUE	0.8465#	

There was no statistically significant correlation between W/H RATIO and SMI.

WAIST CIRCUMFERENCE

SEX AND WAIST CIRCUMFERENCE

Among the 44 females 30 (68.18%) of them having high waist circumference and only 13 (23.21%) out of the 56 males having WC on the high side. Females having high waist circumference compared to males.

TABLE 11: SEX AND WAIST CIRCUMFERENCE

SEX	WAIST CIRCUMFERANCE			
	NORMAL		HIGH	
	NO	%	NO	%
MALES (56)	43	76.79	13	23.21
FEMALES (44)	14	31.82	30	68.18
P VALUE	<0.0001****			

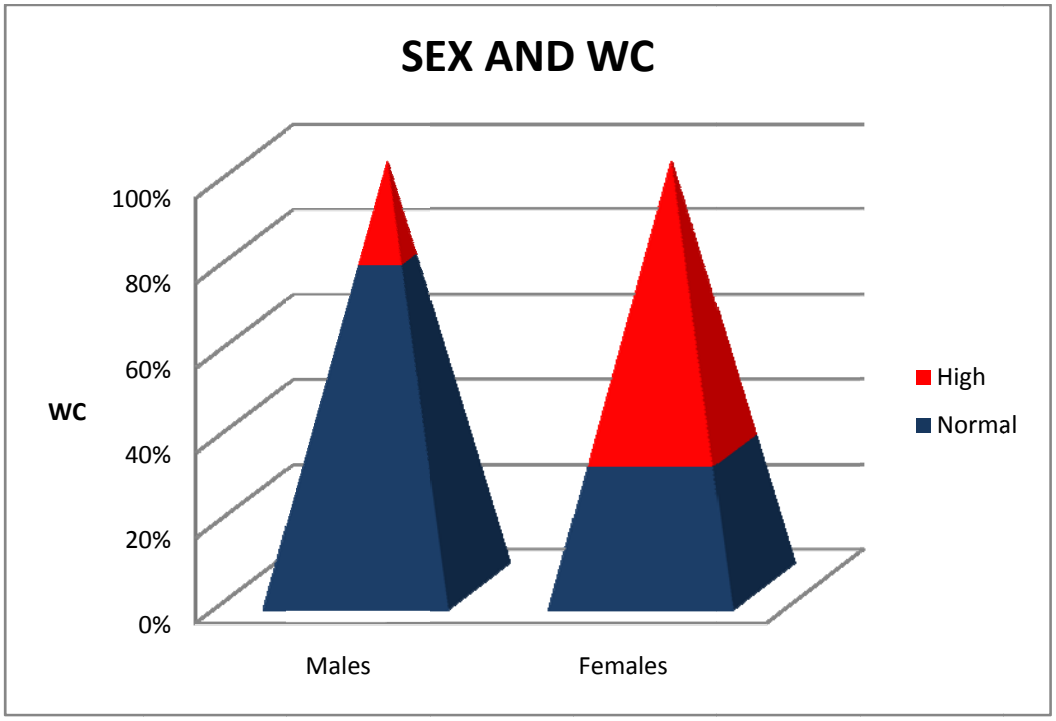
There was a statistically significant correlation between sex and WC.

TABLE 12: WC AND SMI

WC	NO SMI	YES SMI
MEAN±S.D.	83.46±8.09	88.59±12.65
P VALUE	0.0346*	

There was a statistically significant positive correlation WC and SMI.

GRAPH 6 : SEX AND WAIST CIRCUMFERENCE



HbA1c:

HbA1c AND SEX

Among the 56 males 44(78.57%) of them have HbA1c ≥7 and 33 (75%) out of the 44 females were having HbA1c ≥ 7.

Eventhough it appears as males having poor control of blood sugar than males the difference was not statistically significant.

TABLE 13: SEX AND HbA1c

SEX	HbA1c			
	<7		≥7	
	NO	%	NO	%
MALES (56)	12	21.43	44	78.57
FEMALES (44)	11	25	33	75
TOTAL (100)	23		77	
P VALUE	0.8114#			

HbA1c AND DURATION OF DIABETES

Out of the 47 patients who had diabetes for more than 5 years 43(91.49%) patients have HbA1c ≥7 compared to 53 of the diabetics of less than 5 years only 34 (64.15%) of them have HbA1c ≥7.

As duration of diabetes increases many of the patients have not in good control of blood sugar and it was statistically significant.

TABLE 14 : DURATION OF DM AND HbA1c

DURATION OF DM (YEARS)	HbA1c			
	<7		≥7	
	NO	%	NO	%
≤5	19	35.85	34	64.15
>5	4	8.51	43	91.49
TOTAL	23		77	
P VALUE	0.0016**			

GRAPH 7: DURATION OF DM AND HbA1c

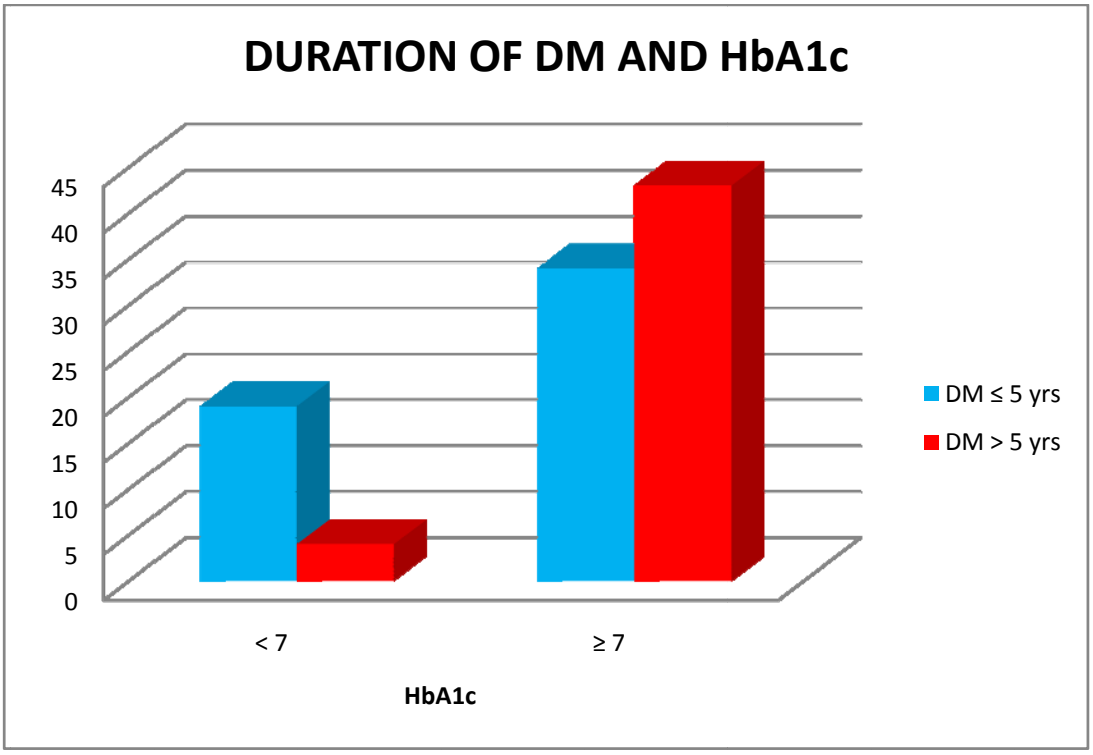


TABLE 15 : HbA1c AND SMI

HbA1c	NO SMI	YES SMI
MEAN±S.D.	7.57±1.1031	8.51±1.1459
P VALUE	0.0021**	

There was a statistically significant correlation between HbA1c and SMI.

DYSLIPIDEMIA:

SEX AND DYSLIPIDEMIA

Among the 100 patients studied 55 of them having dyslipidemia.

50% dyslipidemic in males and 61.36% dyslipidemic among females.

Females have more dyslipidemia compared to males but the difference was not statistically significant.

TABLE 16 : SEX AND DYSLIPIDEMIA

LIPIDS	MALES		FEMALES	
	NO	%	NO	%
NORMAL	28	50	17	38.64
DYSLIPIDEMIA	28	50	27	61.36
TOTAL	56		54	
P VALUE	0.3130#			

DURATION OF DM AND DYSLIPIDEMIA

Among the 47 patients in DM of more than 5 years category 38 (80.85%) of them having dyslipidemia compared to only 17 (32.08%) out of 53 of them in the DM less than and equal to 5 years category.

Dyslipidemia was more common in DM of more than five years duration.

This difference was statistically significant.

TABLE 17: DURATION OF DM AND DYSLIPIDEMIA

DURATION OF DM (YRS)	DYSLIPIDEMIA				TOTAL
	YES		NO		
	NO.	%	NO.	%	
≤5	17	32.08	36	67.92	53
>5	38	80.85	9	19.15	47
TOTAL	55		45		100
P VALUE	<0.0001****				

GRAPH 8 : DYSLIPIDEMIA AND DURATION OF DM

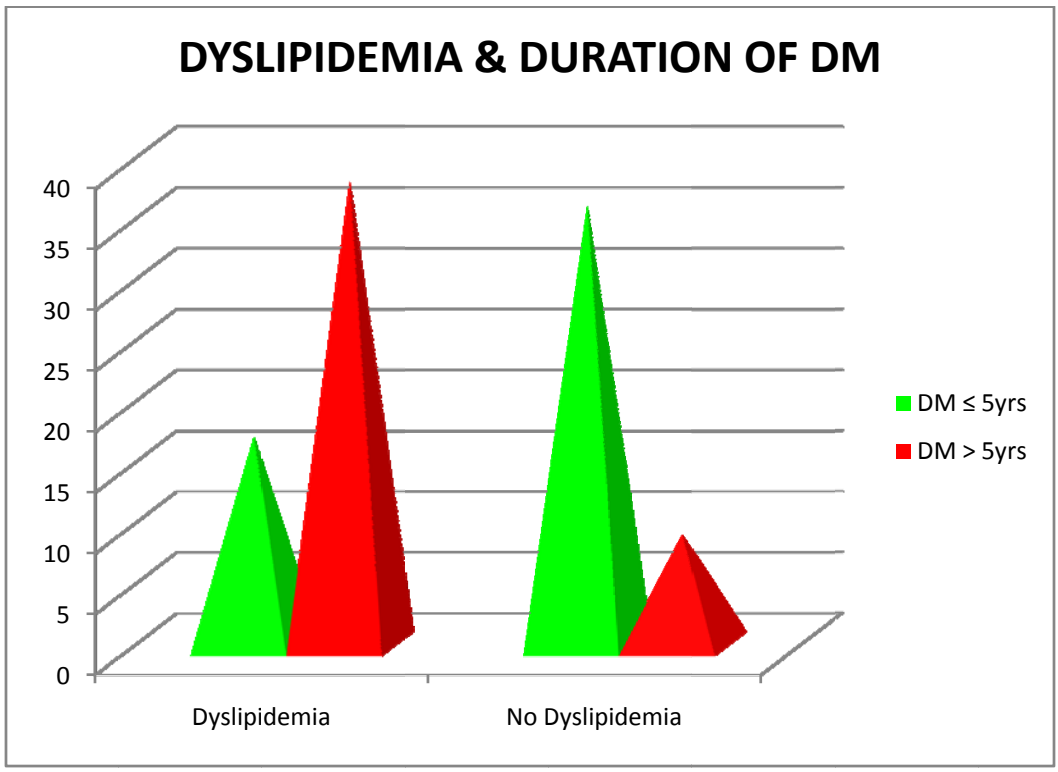


TABLE 18: DYSLIPIDEMIA AND SMI

	NO SMI	YES SMI
DYSLIPIDEMIA	40 (48.19%)	15 (88.24%)
P VALUE	0.0027**	

SMI was more common in DM patients with dyslipidemia.

There was a statistically significant positive correlation between dyslipidemia and SMI.

ABI

Among the 100 patients studied only 14 of them having low ABI (≤0.9).

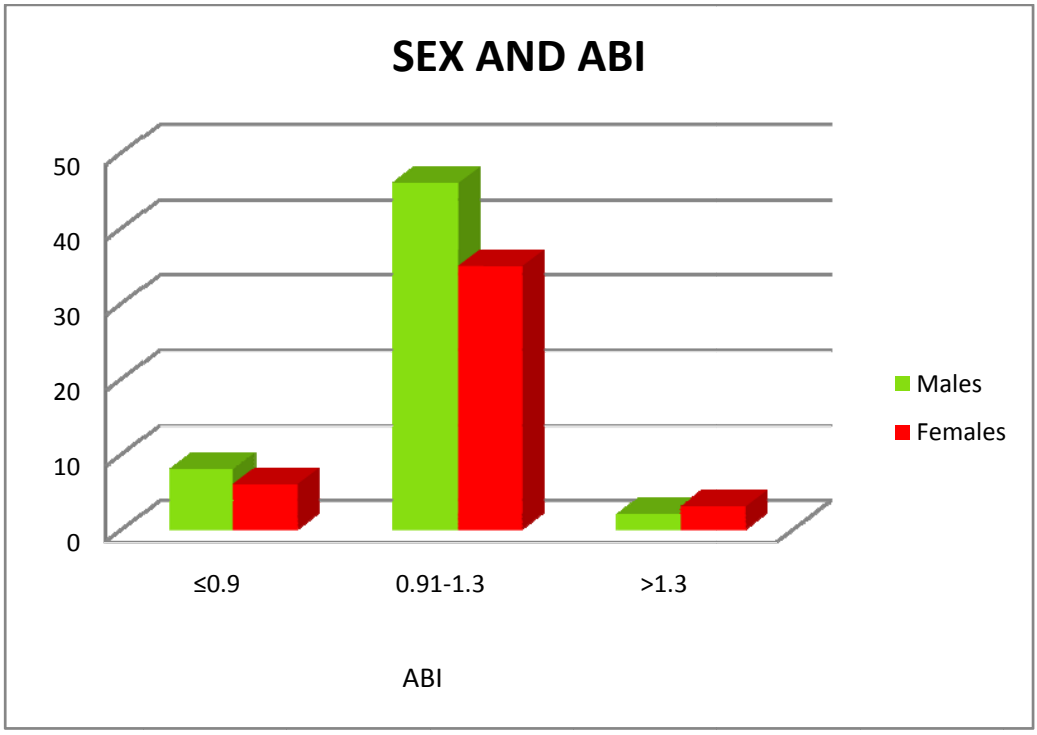
81 of them belongs to normal ABI (0.91-1.3) category and the remaining 5 of them belongs to high ABI (>1.3) category.

There was not much significant difference between males and females.

TABLE 19: SEX AND ABI

ABI	MALES		FEMALES	
	NO	%	NO	%
≤0.9	8	57.14	6	42.86
0.91-1.3	46	56.79	35	43.21
>1.3	2	40	3	60

GRAPH 9 : SEX AND ABI



ABI AND DURATION OF DIABETES

Among the 100 patients studied all 14 patients having low ABI (≤0.9and all the 5 patients having high ABI) belongs to DM >5years duration category.

All of the remaining 53 patients having normal ABI have DM ≤5years duaration.

TABLE 20: ABI AND DURATION OF DM

DURATION OF DM(YEARS)	ABI	
	≤0.9	>0.9
≤5	0	53
>5	14	33
P VALUE	<0.0001****	

As duration of DM increases ABI value decreases and there was statistically significant correlation between them.

ABI AND HbA1c

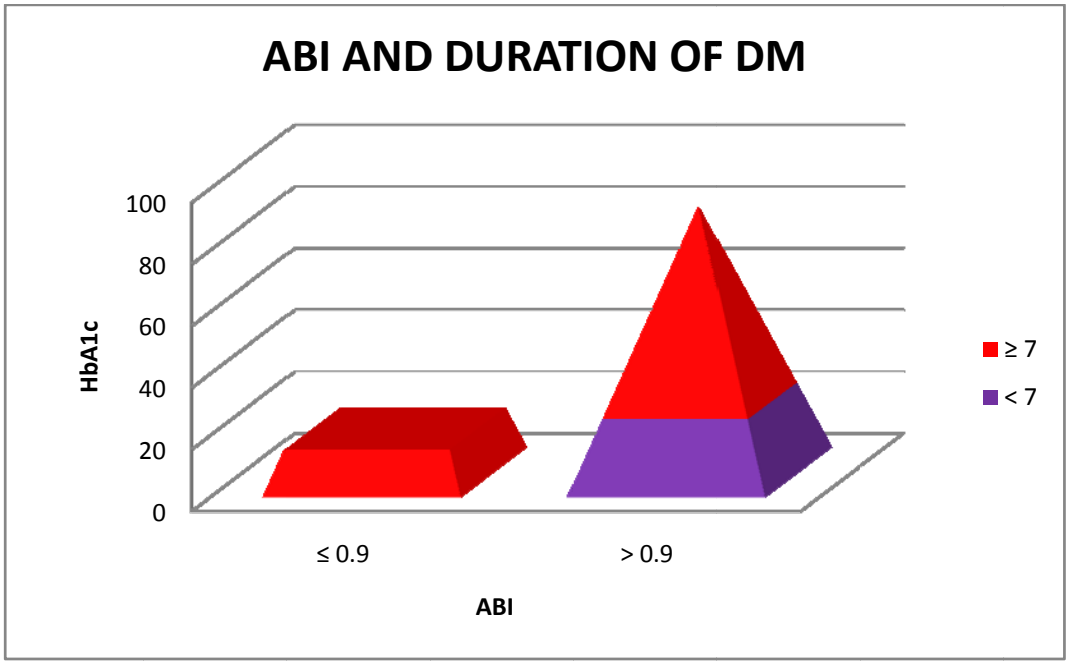
Among the 14 patients having ABI ≤0.9, all the 14 (100%) belongs to HbA1c ≥7 category and out of the 86 patients having ABI >0.9 only 63 (73.26%) belongs to HbA1c ≥7 category.

There was a significant correlation between ABI and HbA1c.

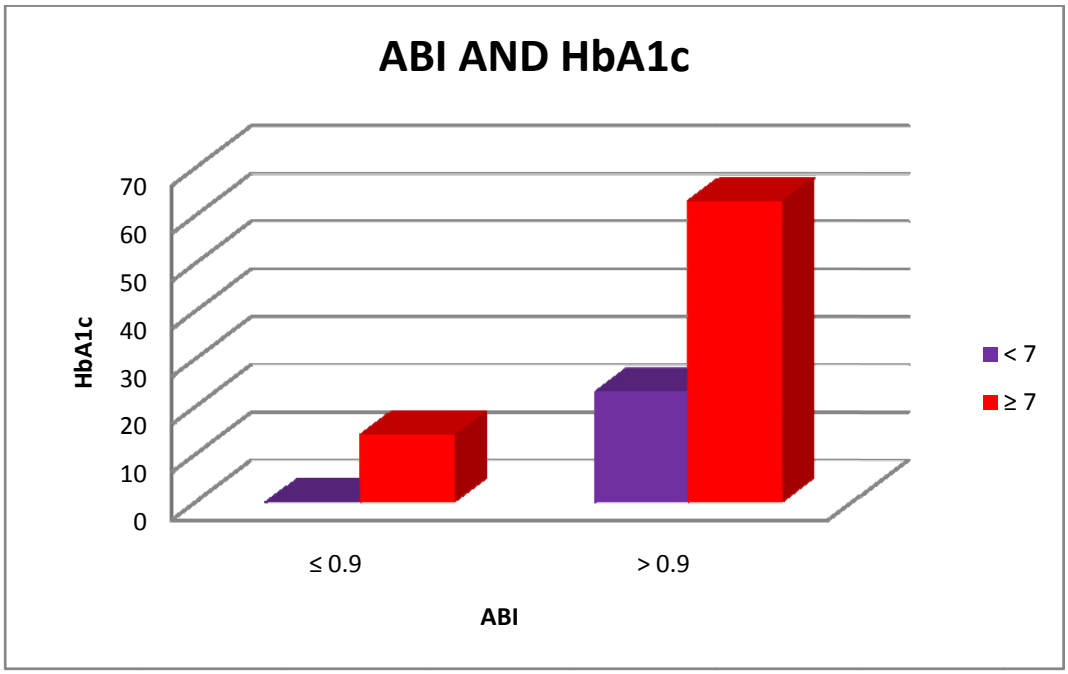
TABLE 21: ABI AND HbA1c

HBA1c	ABI			
	≤0.9		>0.9	
	NO	%	NO	%
<7	0	0	23	26.74
≥7	14	100	63	73.26
TOTAL	14		86	
P VALUE	0.0354*			

GRAPH 10 : ABI AND DURATION OF DM



GRAPH 11 : ABI AND HbA1c



TMT

Among the 100 patients studies 17 have positive TMT AND 83 have negative TMT.

TABLE 22 : TMT

TMT	NO. OF PATIENTS	PERCENTAGE (%)
POSITIVE	17	17
NEGATIVE	83	83

SEX AND TMT

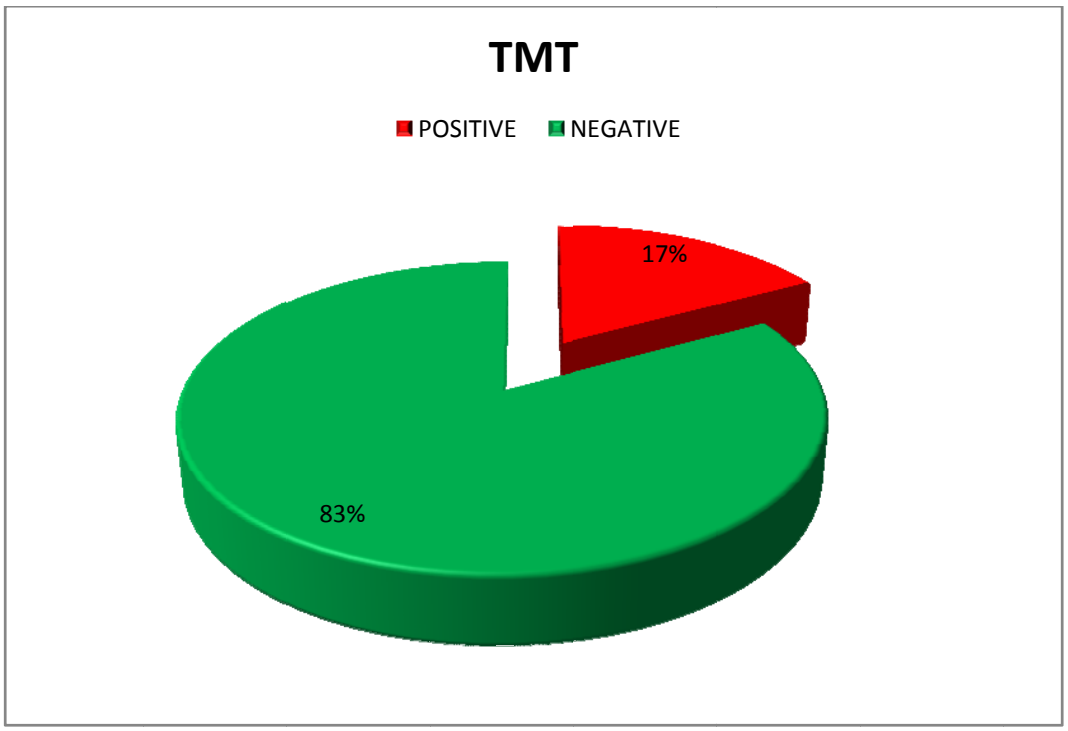
Among the 17 patients having positive TMT 10 (58.82%) were males and 7 (41.18%) were females.

Although it appears as males have more TMT positivity this difference was not statistically significant.

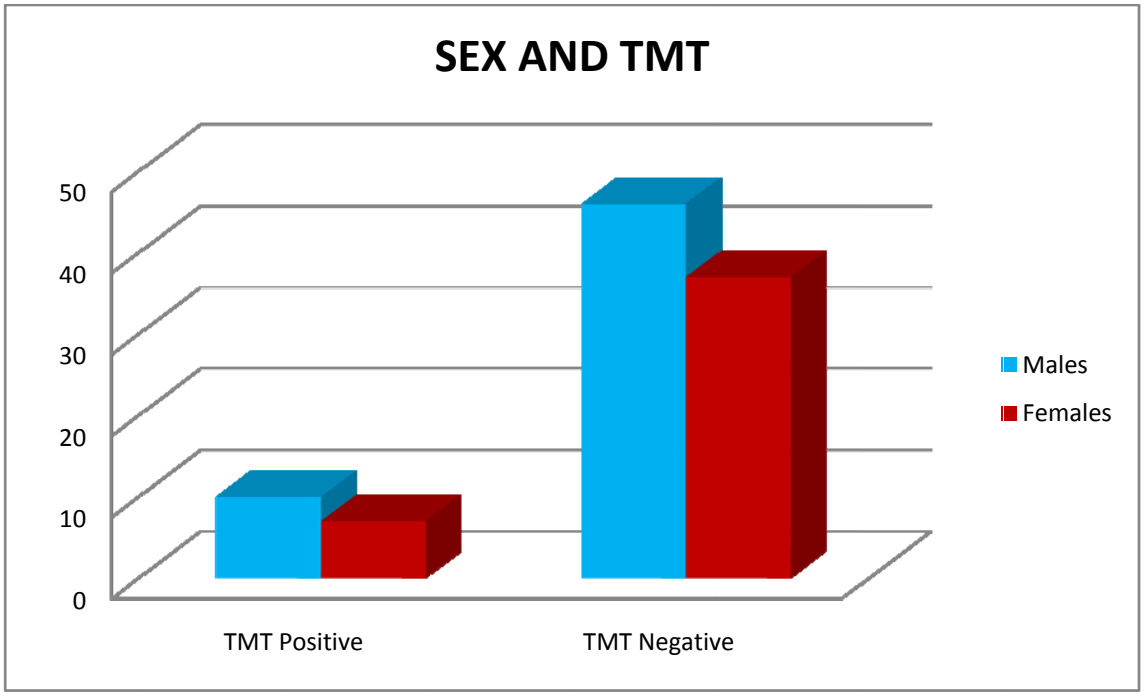
TABLE 23 : SEX AND TMT

TMT	MALES		FEMALES	
	NO	%	NO	%
POSITIVE	10	58.82	7	41.18
NEGATIVE	46	55.42	37	44.58
P VALUE	1.000#			

GRAPH 12 : TMT RESULTS



GRAPH 13 : SEX AND TMT



TMT AND DURATION OF DM

All of the 17(100%) patients having POSITIVE TMT belong to DM of >5 years duration and only 30 (36.14%) out of the 83 TMT NEGATIVE patients belongs to DM of >5 years.

As the duration of the diabetes increases the TMT positivity also increase and this was highly significant statistically.

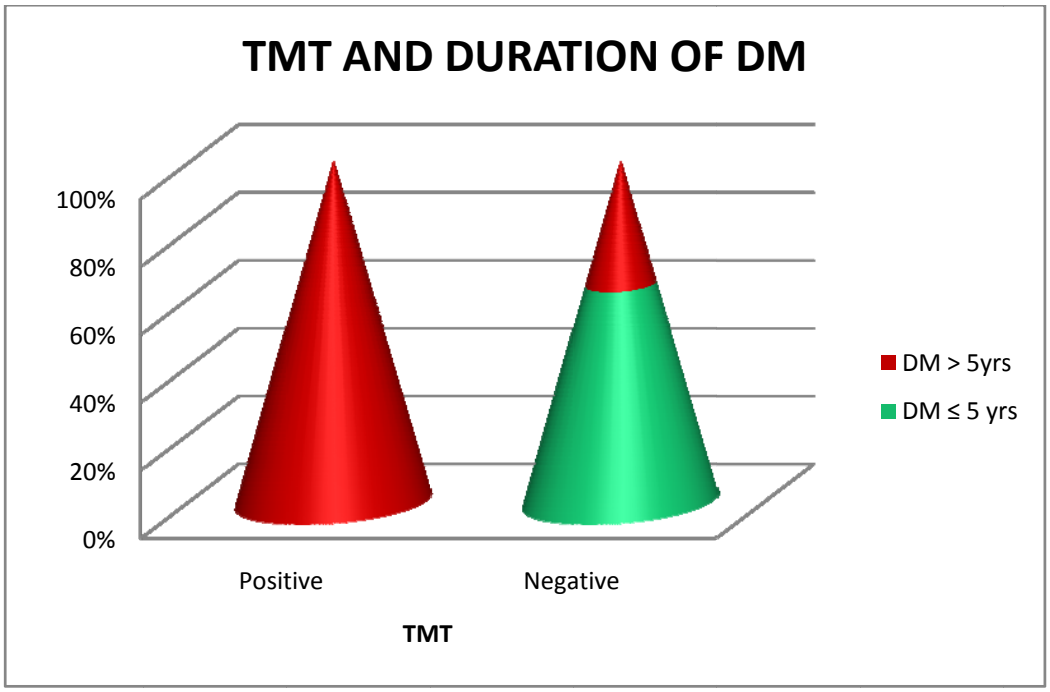
TABLE 24: TMT AND DURATION OF DM

DURATION OF DM (YEARS)	TMT			
	POSITIVE		NEGATIVE	
	NO	%	NO	%
≤5	0	0	53	63.86
>5	17	100	30	36.14
TOTAL	17		83	
P VALUE	<0.0001****			

TABLE 25: DURATION OF DM AND SMI

DURATION OF DM (years)	NO SMI	SMI
MEAN±S.D.	5.13±3.38	11.41±3.45
P VALUE	<0.0001****	

GRAPH 14 : TMT AND DURATION OF DM



ABI AND TMT

Among the 17 TMT POSITIVE patients 14 (82.35%) of them have ABI ≤0.9 and among the 83 TMT NEGATIVE patients all of the have ABI >0.9.

As ABI decreases ≤0.9 the TMT POSITIVITY RATE increases and this was highly significant statistically.

There was no statistically significant difference between the normal ABI (0.91-1.3) group and the high ABI (>1.3) group in terms of TMT POSITIVITY.

TABLE 26: ABI AND TMT

ABI	TMT			
	POSITIVE		NEGATIVE	
	NO	%	NO	%
≤0.9	14	87.50	0	0
0.91-1.3	2	12.50	79	100
TOTAL	16		79	
P VALUE	<0.0001****			

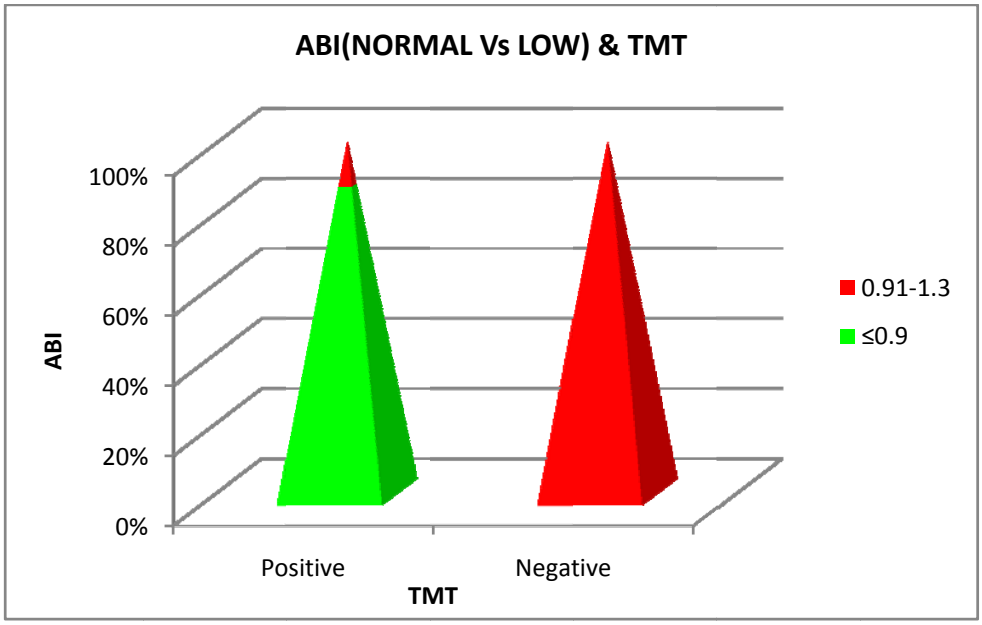
TABLE 27: ABI AND TMT

ABI	TMT			
	POSITIVE		NEGATIVE	
	NO.	%	NO.	%
0.91-1.3	2	66.67	79	95.18
>1.3	1	33.33	4	4.82
TOTAL	3		83	
P VALUE	0.1663#			

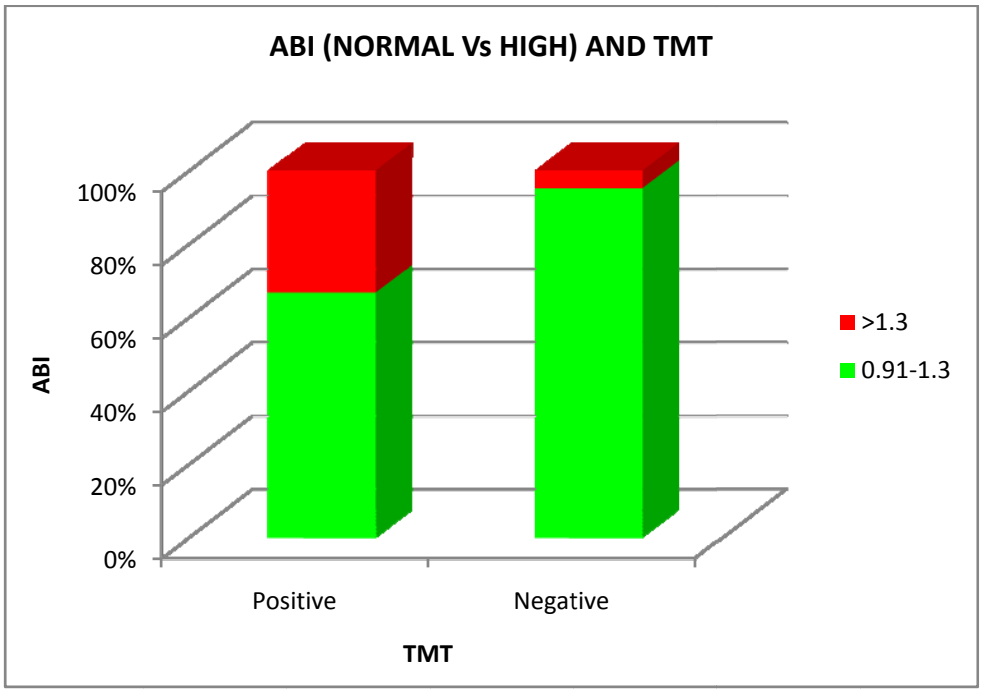
TABLE 28: ABI AND SMI

ABI	NO SMI	YES SMI
MEAN±S.D.	1.14±0.09	0.87±0.19
P VALUE	<0.0001****	

GRAPH 15 : ABI (NORMAL Vs LOW)AND TMT



GRAPH 16 : ABI (NORMAL Vs HIGH)AND TMT



BASELINE CHARACTERISTICS OF THE STUDY POPULATION

PARAMETER	NO SMI	YES SMI	P VALUE
No. of Patients	83	17	
Age *(years)*	49.87±6.22	54.24±3.11	0.0059**
DM Duration*(Years)*	5.13±3.38	11.41±3.45	<0.0001****
BMI	22.56±3.5	22.56±3.5	<0.0100***
W/H RATIO	0.8917±0.07	0.8882±0.01	0.8465#
WC	83.46±8.09	88.59±12.65	0.0346*
Dyslipidemia(n(%))	40(48.19%)	15(88.24%)	0.0027**
Hypertension(n(%))	32(38.55%)	11(64.71%)	0.0613#
Smoking(n(%))	27(32.53%)	7(41.18%)	0.5768#
Alcoholism(n(%))	30(36.14%)	5(29.41%)	0.7815#
HbA1c	7.57±1.1031	8.51±1.1459	0.0021**
ABI	1.14±0.09	0.87±0.2	<0.0001****

* – SIGNIFICANT (p < 0.05), ** – VERY SIGNIFICANT (p<0.01), *** – HIGHLY SIGNIFICANT (p<0.001), **** – VERY HIGHLY SIGNIFICANT (p<0.0001), # – NOT SIGNIFICANT

Results are reported as Mean ± Standard deviation and as mean with range wherever applicable. Difference between means for parametric data was calculated using the student's unpaired t-test with two tailed p value. Difference between means for non-parametric data was calculated using Mann-Whitney test with two tailed p value. Difference between proportions was calculated using Fisher's exact test with two tailed p value.

DISCUSSION

AGE

In our study of 100 patients majority of them (91%) of them belongs to 41-50 years age group. In our study we found that the average age for patients with SMI was 54.24±3.11 and without SMI was 49.87±6.22. As age increases chance of getting SMI also increases in type DM patients and there was stastistically significant correlation between the two with P value of 0.0059.

In DIAD STUDY[107] they found that the age for the patients with SMI ranges from 61- 64years . Compared to that study the average age at which SMI was diagnosed was lower in our study. In another study conducted in Turkish population by Ugur-Altun B et al[108] they found that the average age in SMI group was 55±3 which was almost nearer to our study. In another study conducted by Kim MK et al[109] the average age group in patients with SMI was 63.1±9.4 and compared to this study the age group was lower in our study.

GENDER

In our study of 100 patients 56 were males and 44 were females. Among the 17 patients having positive TMT 10 (58.82%) were males and 7 (41.18%) were females. Although it appears as males have more TMT positivity this difference was not statistically significant.

In DIAD STUDY[107] they found that men have more SMI in the form of large perfusion abnormality than women.Ugur-Altun B et al[108] found in their study that no sex preference in patients with SMI. The prevalence of SMI was almost similar in both males and females in a study done by AK Agarwal et al[110] in New Delhi.

HYPERTENSION

Among the 100 patients studied 43 had hypertension. Majority of the hypertensive were males 26(60.47%). Largest number of hypertensive 25(58.14%) were in the 51-60 age group. Among the 17 SMI patients 11 were having hypertension. Even though it appears as SMI was common in patients with associated SHT there was no statistically significant correlation between them with a P value of 0.0613.

In a study done by Lubaszewski W et al[111] they found that SMI was more frequent in patients with type 2 DM and essential hypertension.

ACTIVE SMOKING

Out of the 56 males 34 (60.71%) were active smokers. None of the females were active smokers. Of the 17 patients having SMI only 7 of them were active smokers and there was no statistically significant correlation between smoking and SMI with a P value of 0.5768. The cardiovascular burden of diabetes increases in combination with smoking.

In DIAD study[107] they found that active smoking have no significant impact on SMI. In a study by AK Agarwal et al[110] the

prevalence of smoking in SMI is 9.1% and no correlation with SMI statistically.

ALCOHOLISM

Among the 100 patients studied only male alcoholics were found. Out of the 56 males 35 (62.5%) were alcoholics. In our study out of the 17 SMI patients only 5 were alcoholic and 12 were non alcoholic and there was no significant correlation between the two with a P value of 0.7815.

In DIAD study[107] they found that alcoholism has no significant impact on SMI. In AK Agarwal et al[110] study the prevalence of heavy alcohol consumption was 9.1%. and there were more alcoholics in the NON SMI group similar to in our study.

BODY MASS INDEX

Among the 100 patients studied 49 of them belongs to overweight and obese category and 51 of them belongs to normal and underweight category. As age increases there was no significant increase in BMI and majority 31(60.78%) of the 51-60 years age group were normal and underweight. There was no statistically significant relation between age and BMI with a P value of 1. Among the 56 males in my study 30(53.57%) belongs to normal and underweight category and the remaining 26 (46.43%) belongs to overweight and obese category.

Among the 44 females i have studied 23 (52.27%) of them belongs to overweight and obese category and the remaining 21 (47.73%) of them belongs to normal and underweight category. There was a slight increase in BMI among females compared to males and this was not signifiant statistically with a P value of 0.6873. The mean BMI in patients with SMI was 25.52±1.664 and that of the NON SMI group was 22.56±0.3841 and this difference was statistically significant with a P value of 0.01.

In DIAD study[107] the average BMI in patients with SMI ranges from 30-32.5 and in our study it was on the lower side. In AK Agarwal et al[110] study in SMI group 54.54% were obese and in NON SMI group 59.26% were obese and this difference not significant statistically. In a study by Gomez Martinez et al[112] they found that the average BMI in SMI and NON SMI groups were 30.6±3.8 and 30.4±4.2 and no significant difference between them.

WAIST HIP RATIO

In our study among the 44 females 37 (84.09%) were having high W/H ratio and only 36 (64.29%) out of the 56 males were having high W/H ratio. Females having high W/H ratio compared to males.There was stasitically significant relationship between sex and BMI.In our study the average W/H ratio in patients with SMI was 0.8882±0.01 and in NO SMI group it was 0.8917±0.07 and there was no statistical significant correlation between W/H ratio and SMI.

In Gomez Martinez et al[112] study they found that the average W/H ratio SMI group was 1.02±0.05 and in NON SMI group it was 1.00±0.06 and no significant relation between them. In AK Agarwal et al[110] study the average W/H ratio in SMI and NON SMI groups were 0.91±0.09 and 0.92±0.01 and not significant statistically.

WAIST CIRCUMFERENCE

In our study among the 44 females 30 (68.18%) of them having high waist circumference and only 13 (23.21%) out of the 56 males having WC on the high side. Females having high waist circumference compared to males. There was statistically significant correlation between sex and WC with a P value of <0.0001. In our study the average WC in patients with SMI was 88.59±12.65 and in NON SMI group it was 83.46±8.09 and there was significant positive correlation between WC and SMI with a P value of 0.0346.

HbA1c

Among the 56 males 44(78.57%) of them have HbA1c ≥7 and 33 (75%) out of the 44 females were having HbA1c ≥ 7.Eventhough it appears as males having poor control of blood sugar than males the difference was not statistically significant with a P value of 0.8114.

In AK Agarwal et al[110] study the average HbA1c LEVEL in males and females were 7.17±1.77 and 7.38±1.18 and not much difference in among them. Out of the 47 patients who had diabetes for more than 5

years 43(91.49%) patients have HbA1c ≥7 compared to 53 of the diabetics of less than 5 years only 34 (64.15%) of them have HbA1c ≥7. As duration of diabetes increases many of the patients have not in good control of blood sugar and it was statistically significant. In our study the average HbA1c level in patients with SMI is 8.51±1.1459 and in NON SMI group was 7.57±1.1031. SMI is common in patients with poorly controlled diabetes and this difference was statistically significant with a P value of 0.0021. In a study done by AK Agarwal et[110] they found that the average HbA1c level in patient with SMI and NON SMI groups were 7.68±1.40 and 7.71±1.71, not much significant difference between them.

DURATION OF DIABETES

All of the 17(100%) patients having SMI belong to DM of >5 years duration and only 30 (36.14%) out of the 83 NON SMI patients belongs to DM of >5 years. In our study the mean duration of DM in SMI group was 11.41±3.45 and that of NON SMI group was 5.13±3.38 and there was statistically significant difference between them. As the duration of the diabetes increases the SMI also increase and this was highly significant statistically with a P value of <0.0001.

In a study done by Kim MK et al[109] they found that the positive predictive value of treadmill test increased to 87.5% in elderly patients ≥60 years with long duration of DM ≥10 years. In a study done by AK Agarwal et al[110] they found that the average duration of DM in patients

with SMI was 11.19±7.06 and that of NON SMI group it was 9.70±5.92 and there was no statistical difference between them.

DYSLIPIDEMIA

Among the 100 patients studied 55 of them having dyslipidemia. 50% dyslipidemic in males and 61.36% dyslipidemic among females. Females have more dyslipidemia compared to males but the difference was not statistically significant with a P value of 0.3130.Among the 47 patients in DM of more than 5 years category 38 (80.85%) of them having dyslipidemia compared to only 17 (32.08%) out of 53 of them in the DM less than and equal to 5 years category. Dyslipidemia was more common in DM of more than five years duration. This difference was statistically significant with a P value of < 0.0001. In our study 88.24% of patients have dyslipidemia in the SMI group and only 48.19% have dyslipidemia in the NON SMI group and there was statistically significant correlation between the two with a P value of 0.0027. Dyslipidemia was more common in patients with SMI.

In a study done by Gomez martinez et al[112] they found that dyslipidemia was more common in NON SMI group but it was not significant statistically.

ANKLE BRACHIAL INDEX

Among the 100 patients studied only 14 of them having low ABI (≤ 0.9).

81 of them belongs to normal ABI (0.91-1.3) category and the remaining 5 of them belongs to high ABI (>1.3) category. There was not much significant difference between males and females.In BARI 2D TRIAL[113] they found that females having low ABI compared to males.

In our study of 100 patients all 14 patients having low ABI (≤0.9and all the 5 patients having high ABI) belongs to DM >5years duration category. All of the remaining 53 patients having normal ABI have DM ≤5years duaration. As duration of DM increases ABI value decreases and there was statistically significant correlation between them with a P value of <0.0001. In BARI 2D TRIAL they stuidied that as duration of DM increases ABI value decreases.

Among the 14 patients having ABI ≤0.9, all the 14 (100%) belongs to HbA1c ≥7 category and out of the 86 patients having ABI >0.9 only 63 (73.26%) belongs to HbA1c ≥7 category. There was significant correlation between ABI and HbA1c with a P value of 0.0354. In BARI 2D TRIAL they found that no significant impact of HbA1c on ABI.

TMT

Among the 100 patients studies 17 have positive TMT AND 83 have negative TMT. Among the 17 TMT POSITIVE patients 14 (82.35%) of them have ABI ≤0.9 and among the 83 TMT NEGATIVE patients all of the have ABI >0.9. In our study we found that the average value of ABI in patients having SMI and NO SMI were 0.87±0.2 and 1.14±0.09

respectively. As ABI decreases ≤0.9 the TMT POSITIVITY RATE increases and this was highly significant statistically with a P value of <0.0001. There was no statistically significant difference between the normal ABI (0.91-1.3) group and the high ABI (>1.3) group in terms of TMT POSITIVITY with a P value of 0.1663.

In a study done by Gomez Martinez et al they found that the average value of ABI in patients having SMI was 0.91±0.21 and in NO SMI group it is 1.04±0.13 and it was significant statistically.

CONCLUSIONS

The conclusions from this study are

1. There was a significant association between low ABI and SMI
2. The prevalence of SMI in our study was 17% as found in most studies.
3. As age increases chance of getting SMI increases in asymptomatic type 2 DM and it was significant statistically.
4. There was no gender preference in SMI in asymptomatic type 2 diabetics.
5. Traditional cardiac risk factors such as hypertension and smoking did not emerge as significantly predictive of abnormal tests.
6. There was a significant association between HbA1c and low ABI in our study in contrast to many studies.
7. Most of the asymptomatic type 2 diabetics having SMI were obese and there was a significant association between BMI, waist circumference and SMI.
8. SMI was common in poorly controlled asymptomatic type 2 DM as there was a significant association between HbA1c and SMI.
9. As duration of DM increases incidence of SMI also increases and there was a significant association between them.

10. Dyslipidemia emerged as one of the important predictor of SMI in asymptomatic type DM in our study and that association was statistically significant.

This study was able to establish that a simple, cost effective and non-invasive investigation like ABI can predict the presence of asymptomatic CAD in type 2 diabetics. This is more relevant in a developing country like India where the economic resources available with the common man preclude other invasive and costlier modalities of screening for asymptomatic patients. Even though the benefits of early detection of the asymptomatic disease and its treatment has not yet yielded a significant benefit to patients in the studies conducted so far, it remains to be decided only after long term studies with larger populations from the community like the DADDY-D trial[113] come to a conclusion. Till then, in the diabetic capital of the world that is India, bearing in mind the simple and effective measures available for primary prevention, it is the only way forward as prevention is always better than the cure.

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ANNEXURE

"ANKLE BRACHIAL INDEX AS A PREDICTOR OF SILENT MYOCARDIAL ISCHEMIA IN ASYMPTOMATIC TYPE 2 DIABETES MELLITUS PATIENTS"

-

PROFORMA

NAME : ADDRESS :

AGE/SEX :

OCCUPATION : PHONE NO.

COMPLAINTS

Chest pain : Y/N

Breathlessness : Y/N

Palpitation : Y/N

Swelling of legs : Y/N

Syncope : Y/N

Claudication in legs Y/N

PAST HISTORY

DM : CAD:

SHT : STROKE/TIA:

CKD : CCF:

Family H/O premature CAD :

PERSONAL HISTORY

Smoker :

Alcoholic :

GENERAL EXAMINATION

BP : PULSE :

WEIGHT: HEIGHT : BMI :

WAIST CIRCUMFERENCE: WAIST/HIP :

CAROTID BRUIT : RENAL BRUIT : FEMORAL BRUIT:

INVESTIGATION

BLOOD SUGAR :

FASTING : POST PRANDIAL :

HbA1C :

S.CREATININE :

FASTING LIPID PROFILE :

TOTAL CHOLESTEROL: TG: HDL: LDL:

USG ABDOMEN :

ECG IN ALL LEADS :

ECHO :

TREAD MILL TEST :

ANKLE BRACHIAL INDEX(ABI) :

MASTER CHART

S.No	NAME	AGE	SEX	DM(yrs)	SHT	CKD	SMOKER	ALCOHOLIC	BMI	WC	W/H	HbA1c	DYSLIPIDEMIA	ABI	TMT
1	PATCHAPPAN	56	M	10	-	-	-	-	20.06	81	0.95	8.3	+	0.72	+
2	GOPAL	54	M	3	-	-	+	+	22.67	87	0.95	6.9	+	1.16	-
3	MOHAN	43	M	6	+	-	-	-	24.22	86	0.94	7.4	+	1.26	-
4	NAZEER	42	M	2	-	-	+	-	23.14	92	0.98	7.1	-	1.2	-
5	PERUMAL	58	M	5	+	-	-	-	23.14	81	0.92	7.9	-	1.21	-
6	DAKSHANAMOORTHY	56	M	15	+	+	+	+	24.11	80	0.97	10.6	+	0.86	+
7	RAMAKRISHNAN	56	M	10	-	-	+	+	16.54	79	0.89	8	+	1.13	-
8	KRISHNAN	53	M	8	-	-	+	+	17.31	78	0.88	7.4	+	1.23	-
9	SAGADEVAN	59	M	15	+	+	+	+	29.68	104	1.01	9.7	+	1.07	-
10	ANGAMUTHU	47	M	2	-	-	+	+	18.64	76	0.84	6.6	-	1.19	-
11	MANI	50	M	10	-	-	+	-	17.77	75	0.84	7.9	+	1.05	-
12	PALANI	57	M	14	-	-	+	+	22.49	89	0.95	7.9	+	0.68	+
13	MUNUSAMY RAJ	52	M	4	+	-	+	+	24.6	92	0.96	7	+	1.12	-
14	VASUDEVAN	40	M	3	-	-	+	+	19.2	87	1.1	6.5	+	1.11	-
15	MOHAN	50	M	10	+	-	-	-	31.14	99	0.87	7.5	+	0.84	+
16	SUBRAMANIYAM	52	M	4	-	-	+	+	23.73	92	0.98	7	+	1.1	-
17	NAINA MOHAMMAD	52	M	5	-	-	-	-	22.37	87	0.96	7.8	-	1.14	-
18	DHAYALAN	42	M	2	-	-	+	+	22.03	86	0.93	6.7	+	1.17	-
19	JEYARAJ	46	M	4	-	-	+	+	23.98	96	0.98	10.1	-	1.1	-
20	THANGARAJ	45	M	1	-	-	+	+	24.8	89	0.92	6.9	-	1.26	-
21	SANGAIAH	55	M	3	+	-	-	-	19.81	81	0.94	7.3	-	1.08	-
22	EGAMBARAM	55	M	10	+	-	+	-	22.6	85	0.95	8.8	+	0.98	-
23	NEELAKANDAN	45	M	1	+	-	+	+	17.7	90	0.97	6.7	-	1.16	-
24	SRINIVASAN	39	M	3	-	-	-	-	23.62	80	1.05	7.7	-	1.16	-
25	MANIVANNAN	42	M	3	-	-	+	+	25.46	93	0.93	7.1	-	1.19	-
26	MOHAN	49	M	5	-	-	+	+	22.37	87	0.96	7.5	+	1.1	-
27	JAYAKRISHNAN	59	M	7	+	-	-	-	26.33	98	1	7.9	-	1.15	+
28	VELAYUTHAM	47	M	5	-	-	-	-	23.45	76	0.9	8.9	-	1.21	-
29	ALBERT	47	M	3	+	-	-	-	20.43	80	0.9	7	-	1.09	-
30	KAMALNADHAN	60	M	3	+	-	+	+	25.01	90	0.88	9.5	-	1.12	-
31	DURAISAMY	55	M	6	+	-	+	-	18.36	71	0.85	8	+	1.03	-
32	NAGAPPAN	48	M	1	-	-	-	+	16.35	71	0.88	6.9	-	1.24	-
33	MADHAVAN	53	M	15	+	-	+	+	25.21	87	0.91	11.5	+	0.69	+
34	GOPI	55	M	8	-	-	+	+	15.24	66	0.89	8.9	+	0.75	+
35	MUNUSAMY	54	M	10	+	-	+	+	20.76	87	0.95	8.7	+	0.96	-
36	RAVI	41	M	6	-	-	-	+	19.83	79	0.92	7.4	-	1.11	-
37	SEKAR	46	M	6	+	-	-	+	25.71	91	0.91	7.7	-	1.06	-
38	CHAND BASHA	49	M	11	+	+	+	-	29.72	98	0.95	8.7	+	0.83	+
39	JAYASANKAR	37	M	4	+	-	-	-	28.93	92	0.95	7.2	+	1.12	-
40	KESAVAMOORTHY	50	M	13	+	+	+	+	23.5	87	0.96	8.6	+	1.38	-

41	KRISHNAMOORTHY	55	M	3	+	-	-	-	23.45	76	0.9	6.6	-	1.14	-
42	RAJAPPA	43	M	4	+	-	+	+	24.14	92	0.98	7.1	-	1.1	-
43	SAMBANATHAN	60	M	5	-	-	-	+	25.01	90	0.88	6.5	-	1.12	-
44	SUBRAMANI	55	M	4	-	-	-	+	24.22	86	0.94	6.9	-	1.18	-
45	SRIRAM	57	M	10	-	-	+	+	22.03	86	0.93	7.9	+	0.87	+
46	GOPAL	57	M	8	+	-	+	+	19.81	79	0.9	7.8	+	0.99	-
47	KRISHNAN	56	M	6	+	-	-	+	20.7	79	0.94	7.5	-	1.07	-
48	RATHINAL	52	M	10	-	-	-	-	20.43	80	0.9	9	+	1.03	-
49	MURUGESAN	45	M	3	-	-	+	+	23.45	76	0.9	6.7	-	1.16	-
50	ARUL	45	M	5	-	-	-	+	18.36	77	0.9	7.6	-	1.16	-
51	KRISHNARAJ	55	M	4	+	-	-	+	20.41	88	0.9	7.1	-	1.1	-
52	SHANMUGAM	59	M	20	+	+	+	-	17.15	74	0.85	9.7	+	1.4	+
53	BALU	54	M	6	-	-	+	+	25.46	93	0.93	7.9	-	1.06	-
54	MOHAMMAD	55	M	7	+	-	-	-	19.81	81	0.94	7	+	0.97	-
55	SHANKAR	53	M	5	-	-	+	+	18.67	75	0.86	7.8	-	1.11	-
56	KOLLAPARI	60	M	2	-	-	+	-	15.82	75	0.93	6.9	-	1.24	-
57	MARY	46	F	12	-	-	-	-	23.91	85	0.85	8.1	+	1.46	-
58	ABOORVAM	58	F	9	-	-	-	-	21.33	85	0.86	8.9	+	1	-
59	SHANTHI	45	F	7	-	+	-	-	19.02	66	0.81	9	+	1.02	-
60	PUSHPA	56	F	1	-	-	-	-	17.98	65	0.77	7.5	+	1.19	-
61	MURUGAMMAL	55	F	15	+	-	-	-	25.11	87	0.84	8.3	+	0.73	+
62	LALITHA	48	F	6	-	-	-	-	27.08	101	1.08	13.8	+	1.12	-
63	KATTAMMAL	56	F	12	+	-	-	-	22.5	74	0.93	7.9	+	1.06	-
64	SARASWATHY	48	F	3	+	-	-	-	22.34	86	0.85	7.8	+	1.26	-
65	SHANTHI	43	F	6	-	-	-	-	28.8	99	0.88	6.3	+	1.09	-
66	AMUDA	50	F	10	+	-	-	-	35.55	100	0.82	7.5	+	0.88	+
67	INDHIRANI	53	F	1	-	-	-	-	18.69	67	0.78	7	+	1.18	-
68	RANI	45	F	5	-	-	-	-	18.73	68	0.78	7.9	+	1.11	-
69	KOUSALYA	50	F	4	+	-	-	-	22.22	81	0.84	7.9	+	1.12	-
70	MUNIYAMMAL	55	F	3	-	-	-	-	22.34	86	0.85	7.5	+	1.19	-
71	NIRANJANA	37	F	1	+	-	-	-	27.88	99	0.88	6.8	+	1.2	-
72	SHAJATHI BEEVI	58	F	6	+	-	-	-	24.77	92	0.85	6	-	1.08	-
73	DAKCHAYINI	50	F	3	+	-	-	-	21.08	74	0.83	7.4	+	1.12	-
74	SAKUNTHALA	50	F	3	+	-	-	-	22.89	79	0.89	8	+	1.09	-
75	VENILA	53	F	13	-	-	-	-	24.77	95	0.83	7.9	+	0.72	+
76	BHUVANESWARI	40	F	1	-	-	-	-	39.87	100	0.82	7.2	+	1.16	-
77	SALAMMAL	55	F	6	-	+	-	-	21.09	81	0.86	8.7	+	1.14	-
78	CHOKKAMMAL	50	F	5	-	-	-	-	19.39	73	0.86	8	-	1.09	-
79	VIMALA	49	F	7	-	-	-	-	22.1	79	0.84	5.2	+	1.09	-
80	MUNNI	40	F	4	-	-	-	-	23.3	81	0.85	6.5	-	1.12	-
81	SARASU	57	F	5	-	-	-	-	25.1	77	0.75	7.9	-	1.06	-
82	ELAVARASI	39	F	4	-	-	-	-	24.77	86	0.86	7.1	-	1.18	-
83	MUTHAMMAL	55	F	7	-	-	-	-	24.44	87	0.82	8.1	-	1.12	-
84	MEERA	45	F	1	-	-	-	-	23.87	85	0.85	7.1	-	1.18	-
85	NOORJAHAN	58	F	4	-	-	-	-	22.5	81	0.82	7.6	-	1.12	-

86	KASIYAMMAL	55	F	9	+	+	-	-	22.1	79	0.84	9	+	0.85	+
87	DEVAGI	55	F	10	+	-	-	-	44.44	121	0.86	7.4	+	1.2	+
88	MALLIKA	55	F	4	+	-	-	-	22.22	79	0.87	7.7	-	1.09	-
89	SAROJA	50	F	6	+	-	-	-	25.96	84	0.77	6.9	-	1	-
90	BALKESH	56	F	15	+	+	-	-	21.08	75	0.76	8.1	+	1.42	-
91	PRIYA	50	F	10	+	-	-	-	24.03	79	0.82	7.8	+	0.81	+
92	KRISHNAVENI	40	F	2	-	-	-	-	22.6	88	0.88	6.9	-	1.16	-
93	DEIVANI	50	F	2	+	-	-	-	24.11	84	0.78	6.1	-	1.12	-
94	KARPAGAVALLI	48	F	5	-	-	-	-	24.77	93	0.84	7.7	-	1.18	-
95	BADMAVATHY	50	F	8	-	-	-	-	22.22	81	0.84	7.3	+	1.02	-
96	BAKIYALAKSHMI	55	F	15	-	-	-	-	21.09	81	0.86	8.5	+	1.4	-
97	DHANABAKKIYAM	53	F	7	-	-	-	-	24.44	87	0.82	7.8	-	0.79	+
98	RADHA	38	F	1	-	-	-	-	24.77	86	0.86	6.2	-	1.2	-
99	MADHI	48	F	1	-	-	-	-	23.3	81	0.85	6.7	-	1.18	-
100	ADHILAKHSMI	57	F	3	+	-	-	-	25.1	84	0.86	6.7	-	1.12	-

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No: 04425305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. Rajkumar .S
PG in MD General Medicine
Madras Medical College, Chennai -3.

Dear Dr. Rajkumar .S

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled " Ankle brachial index as a predictor of silent myocardial ischemia in asymptomatic type 2 diabetes mellitus patients" No. 18042011.

The following members of Ethics Committee were present in the meeting held on 21.04.2011 conducted at Madras Medical College, Chennai -3.

1.	Prof. S.K. Rajan, MD	-- Chairperson
2.	Prof. V. Kanagasabai MD Dean, Madras Medical College, Chennai-3,	-- Deputy chairman
3.	Prof. A. Sundaram, MD Vice Principal , Madras Medical College, Chennai -3	-- Member Secretary
4.	Prof R. Sathianathan MD	-- Member
5.	Prof R. Nandhini, MD Director, Institute of Pharmacology, MMC, Ch-3	-- Member
6.	Prof. Pregna B. Dolia MD Director , Institute of Biochemistry, MMC, Ch-3	-- Member
7.	Prof. C. Rajendiran .MD Director , Institute of Internal Medicine, MMC, Ch-3	-- Member
8.	Thiru. A. Ulaganathan Administrative Officer, MMC, Chennai -3	-- Layperson
9.	Thiru. S. Govindasamy . BA.BL	-- Lawyer
10.	Tmt. Arnold Soulina	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd /. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee